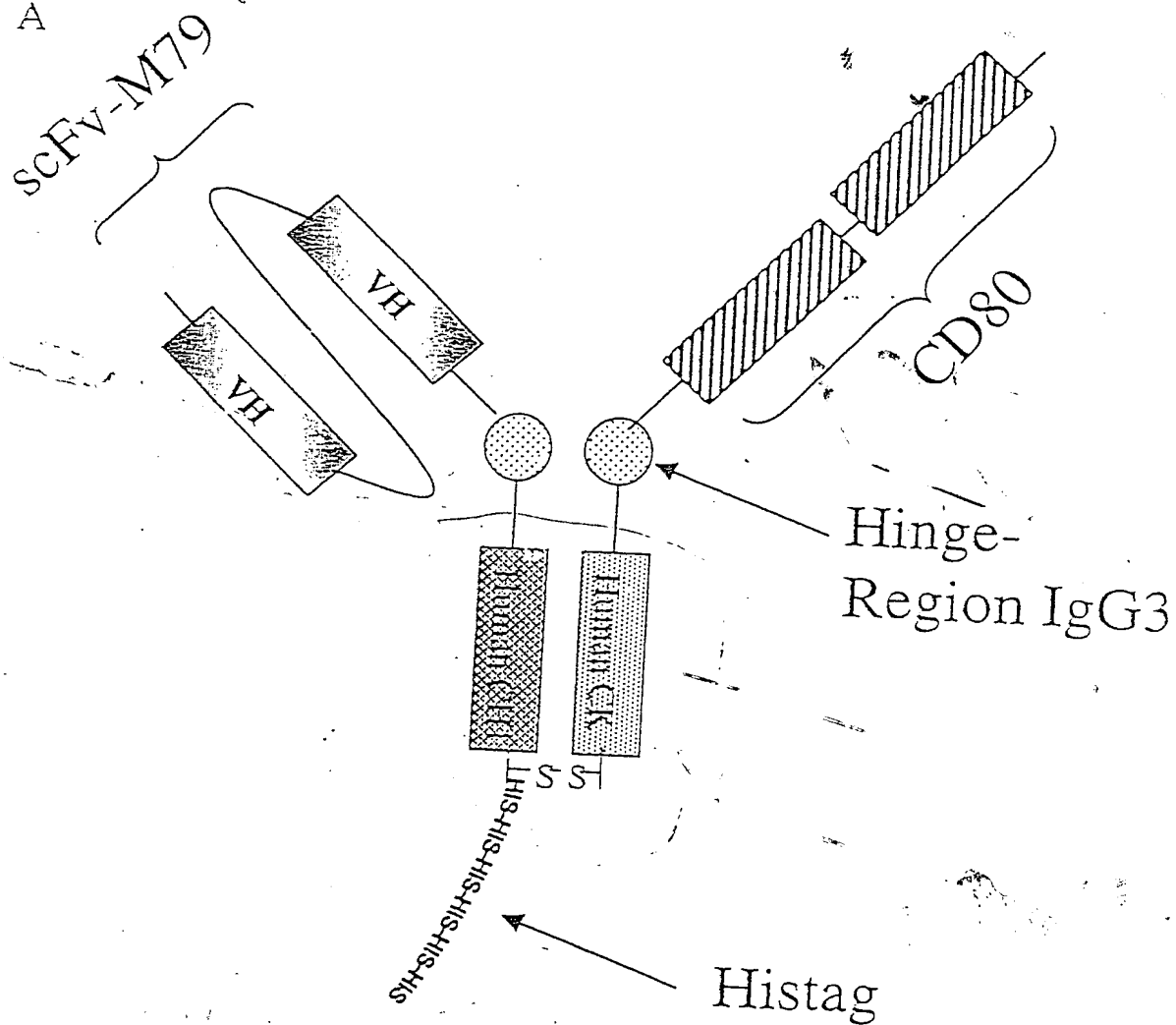
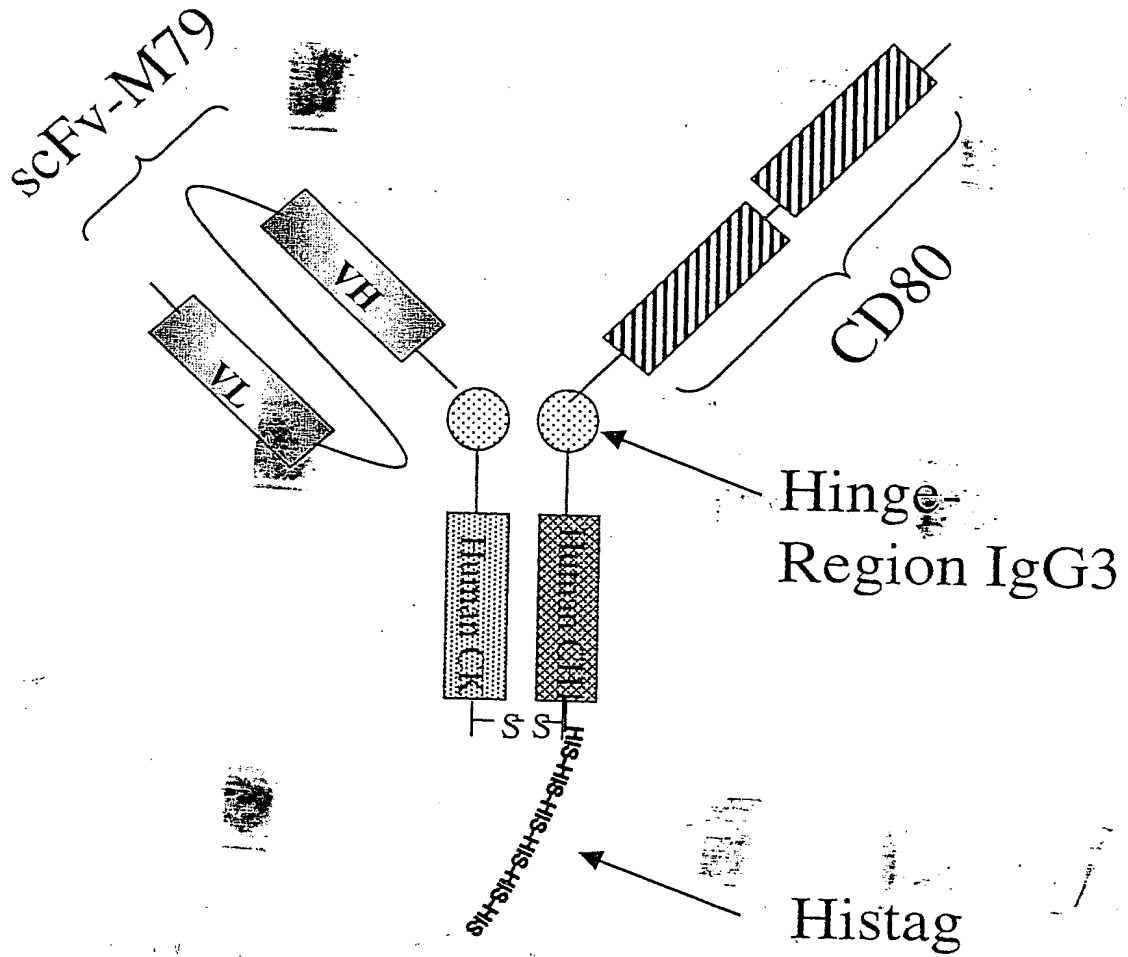


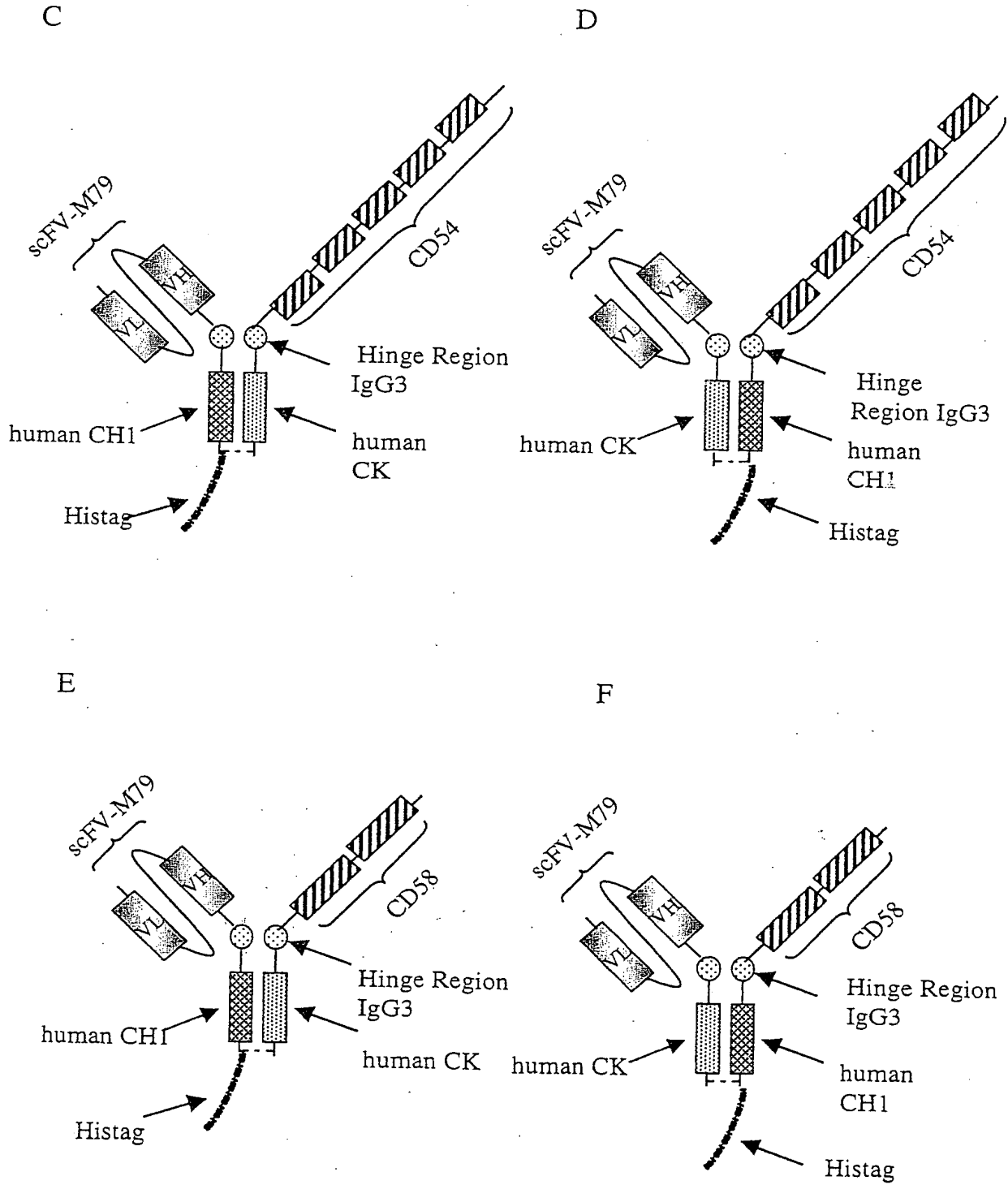
A



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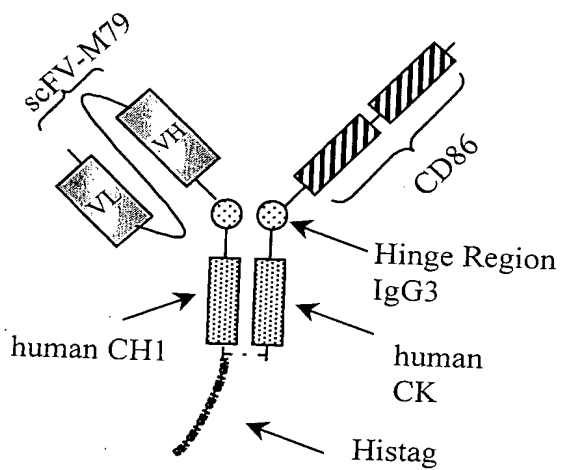
B



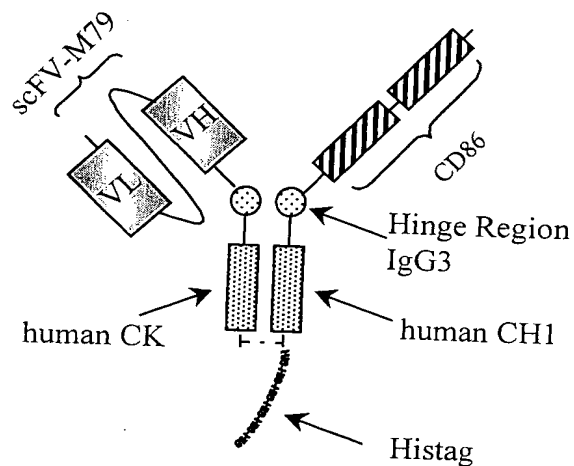


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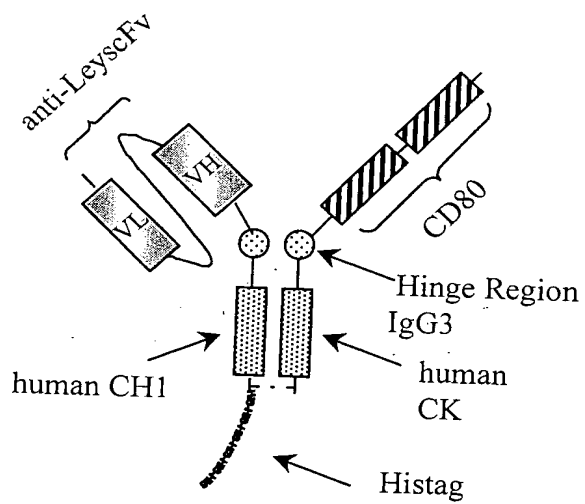
G



H



I



J

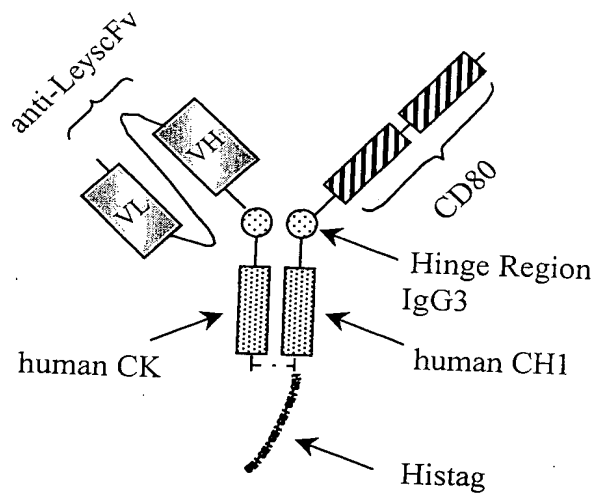
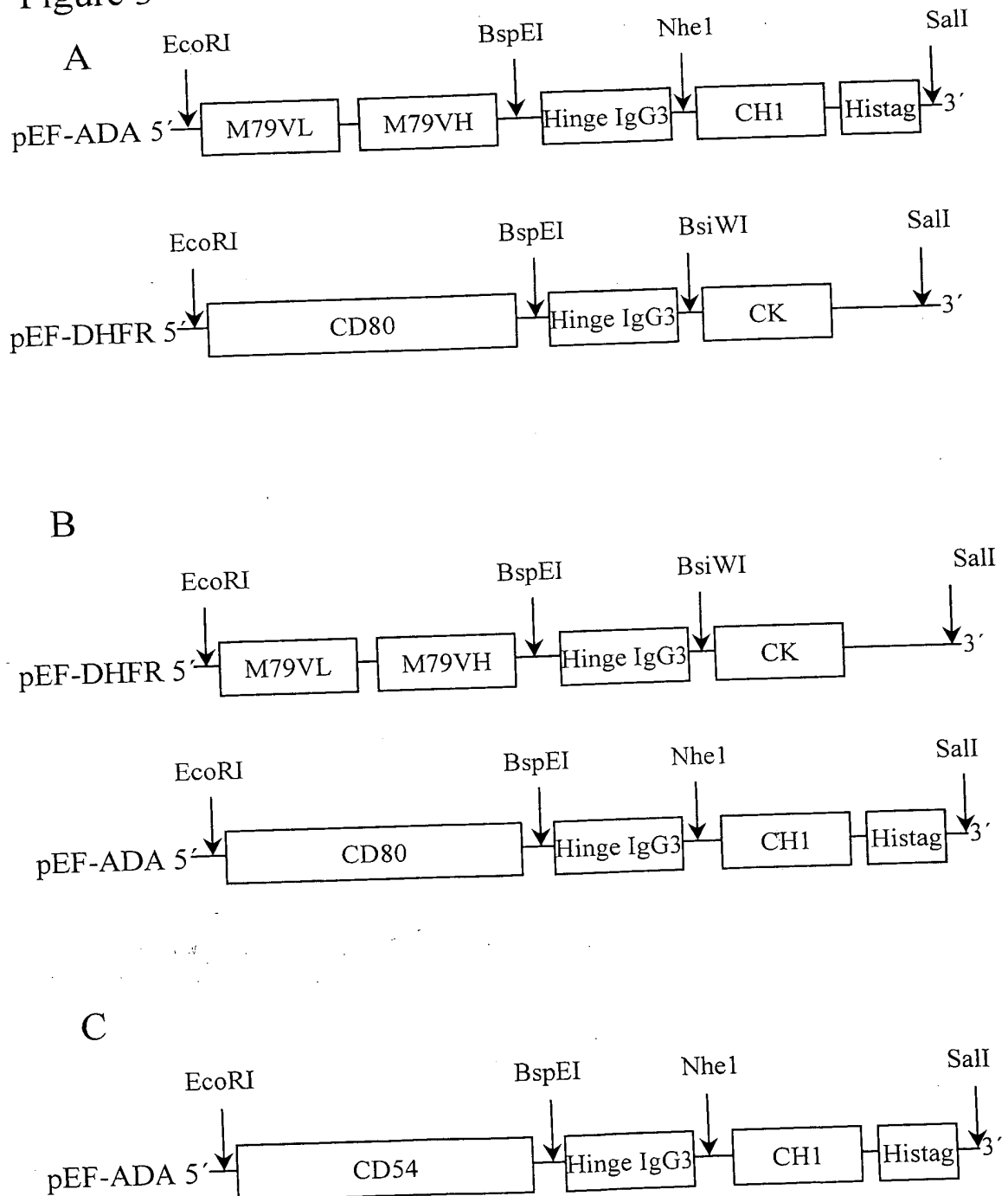


Figure 2

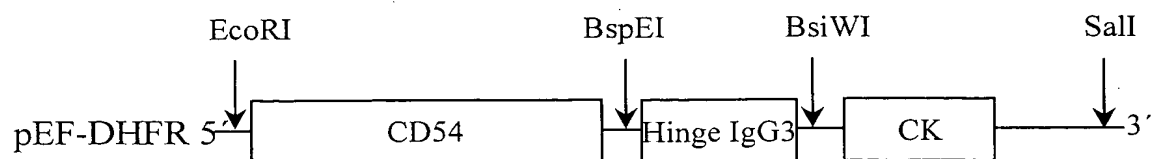
EcoRI
XbaI *AsuII* *BspEI* *BamHI* *EcoRV* *XmaI*
5' CTA GAA TTC TTC GAA TCC GGA GGT GGT GGA TCC GAT ATC CCC GGG
SalI
CAT CAT CAC CAT CAT CAT TGA G 3'

Figure 3

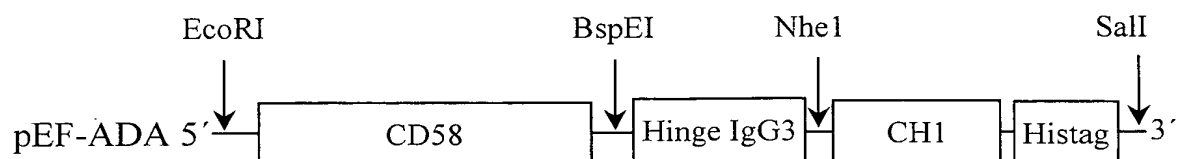


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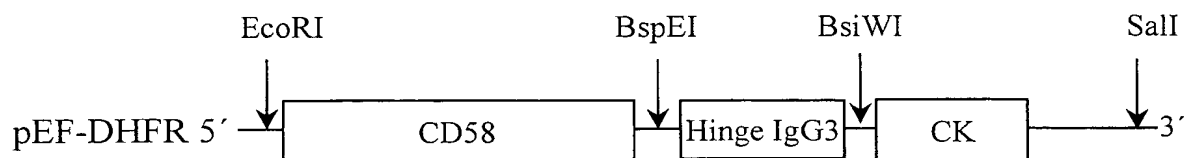
D



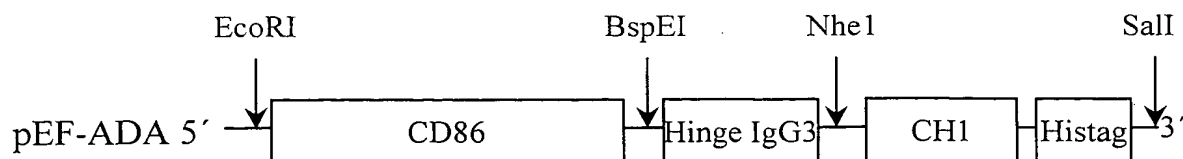
E



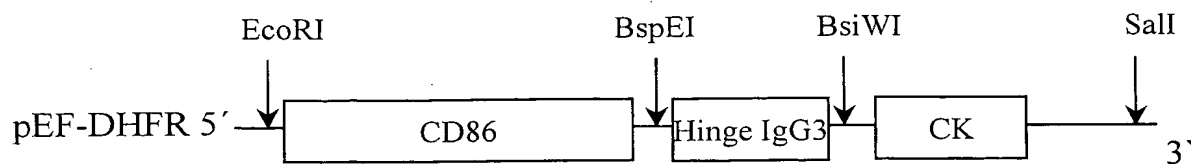
F



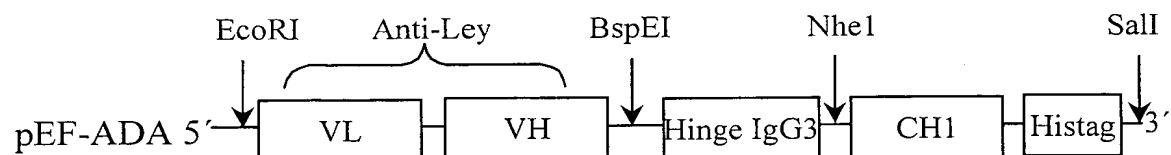
G



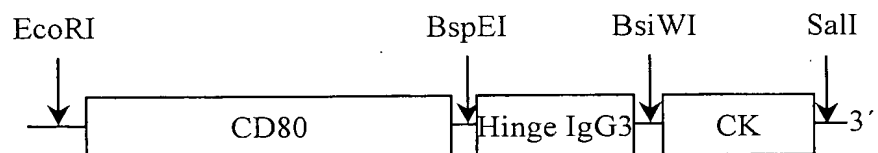
H



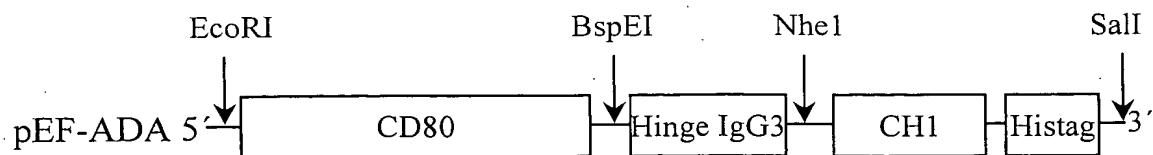
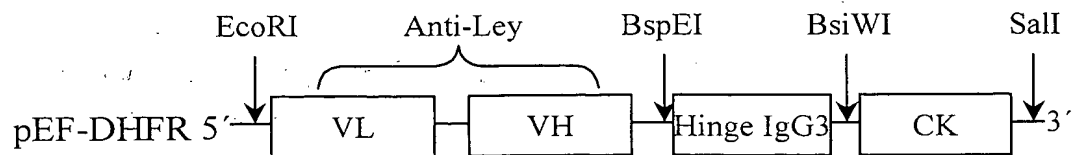
I



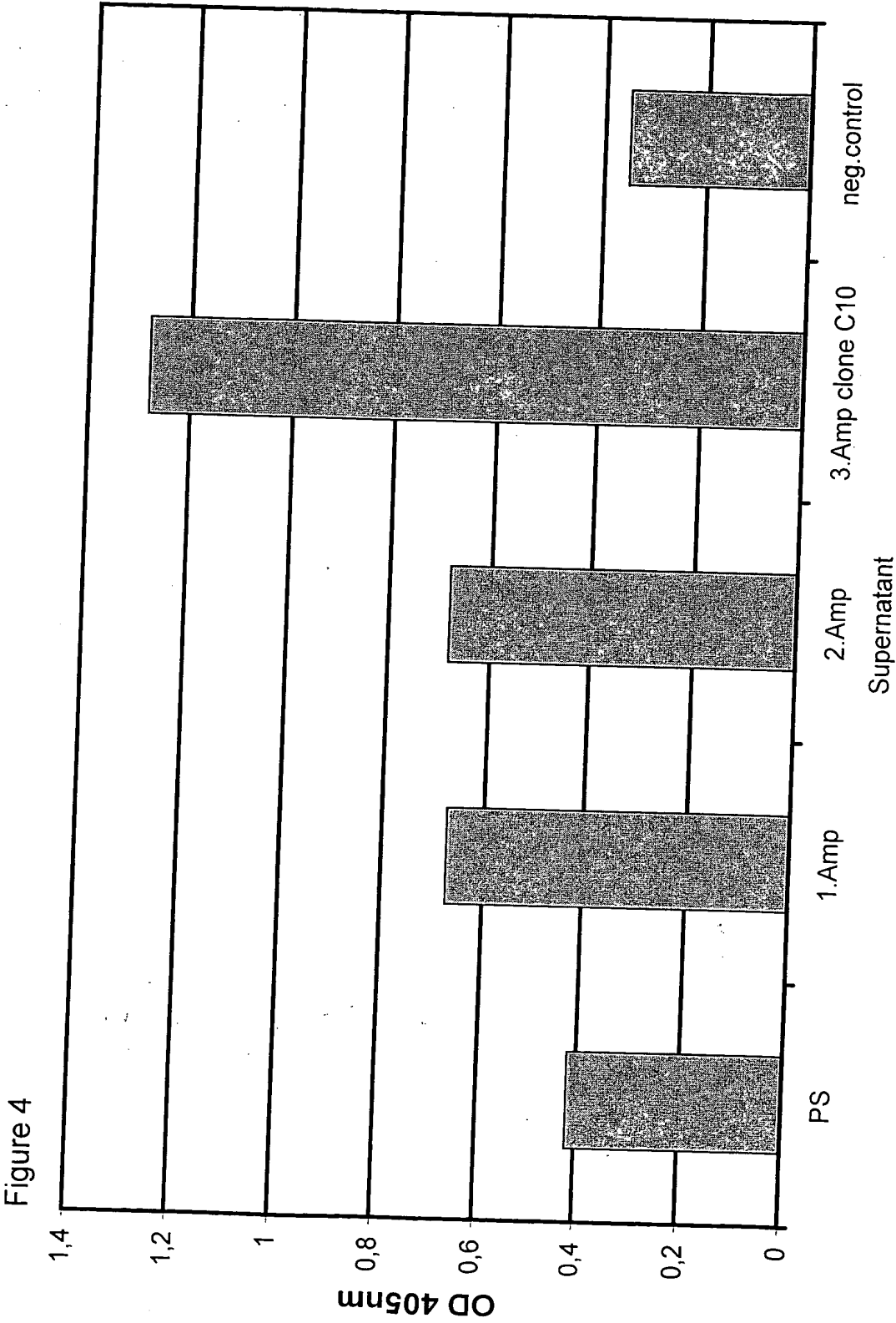
pEF-DHFR 5'



J

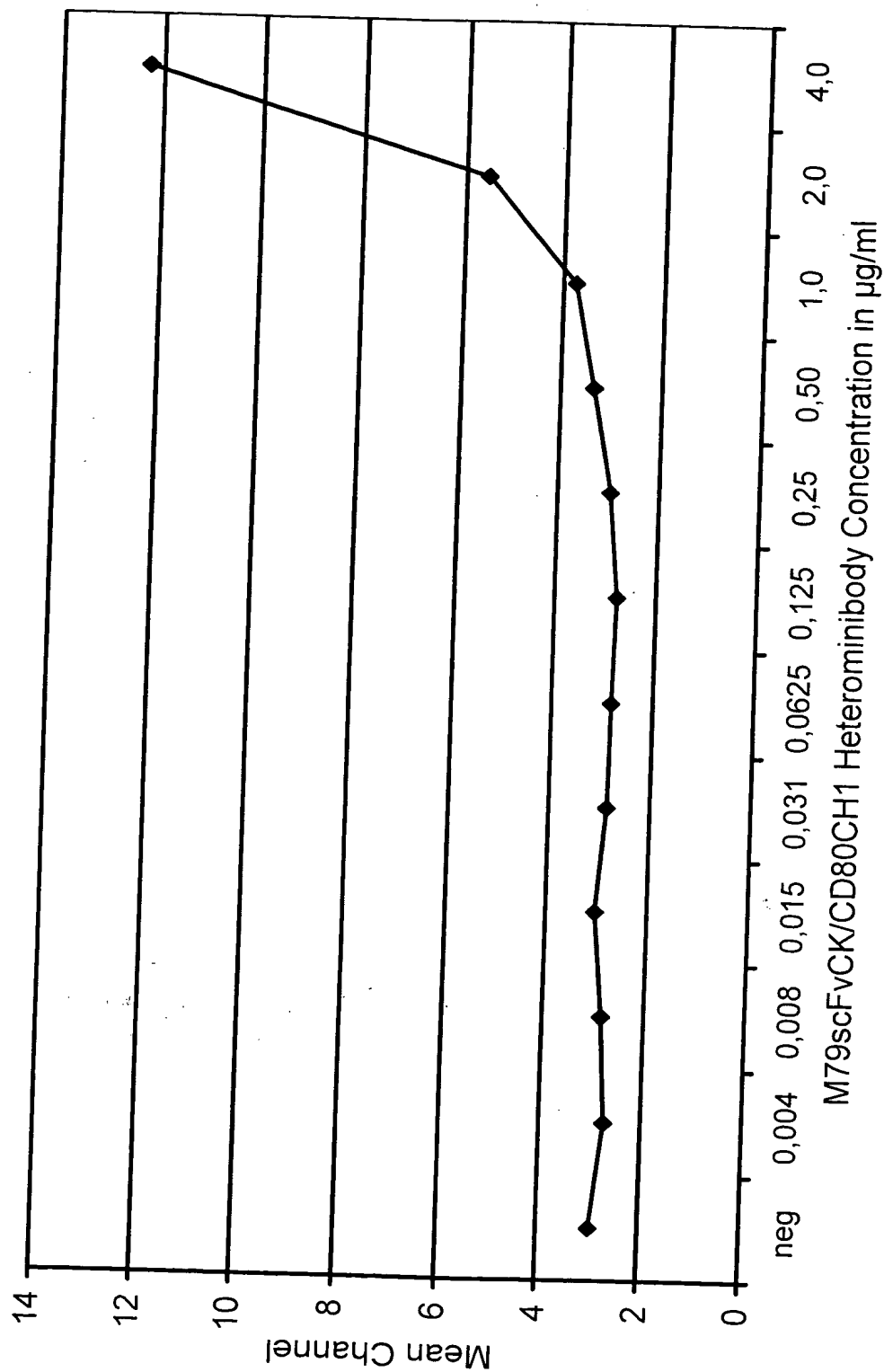


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Figure 5



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Figure 6

<u>ECORI</u>			10	19			28			37			46			55		
5'	GAAT	TCC	ACC	ATG	GGA	TGG	AGC	TGT	ATC	ATC	CTC	TTC	TTG	GTA	GCA	ACA	GCT	ACA
				M	G	W	S	C	I	I	L	F	L	V	A	T	A	T
			64			73			82			91			100			109
	GGT	GTA	CAC	TCC	GAT	ATC	GTT	GTG	ACT	CAG	GAA	TCT	GCA	CTC	ACC	ACA	TCA	CCT
	G	V	H	S	D	I	V	V	T	Q	E	S	A	L	T	T	S	P
			118			127			136			145			154			163
	GGT	GAA	ACA	GTC	ACA	CTC	ACT	TGT	CGC	TCA	AGT	ACT	GGG	GCT	GTT	ACA	ACT	AGT
	G	E	T	V	T	L	T	C	R	S	S	T	G	A	V	T	T	S
			172			181			190			199			208			217
	AAC	TAT	GCC	AAC	TGG	GTC	CAA	GAA	AAA	CCA	GAT	CAT	TTA	TTC	ACT	GGT	CTA	ATA
	N	Y	A	N	W	V	Q	E	K	P	D	H	L	F	T	G	L	I
			226			235			244			253			262			271
	GGT	GGT	ACC	AAC	AAC	CGA	GTT	CCA	GGT	GTT	CCT	GCC	AGA	TTC	TCA	GGC	TCC	CTG
	G	G	T	N	N	R	V	P	G	V	P	A	R	F	S	G	S	L
			280			289			298			307			316			325
	ATT	GGA	GAC	AAG	GCT	GCC	CTC	ACC	ATC	ACA	GGG	GCA	CAG	ACT	GAG	GAT	GAG	GCA
	I	G	D	K	A	A	L	T	I	T	G	A	Q	T	E	D	E	A
			334			343			352			361			370			379
	ATA	TAT	TTC	TGT	GCT	CTA	TGG	TAC	AGC	AAC	CAT	TGG	GTG	TTC	GGT	GGA	GGA	ACC
	I	Y	F	C	A	L	W	Y	S	N	H	W	V	F	G	G	G	T
			388			397			406			415			424			433
	AAA	CTC	GAG	GTC	CTA	GGT	GGT	GGT	GGT	TCT	GGC	GGC	GGC	GGC	TCC	GGT	GGT	GGT
	K	L	E	V	L	G	G	G	G	S	G	G	G	G	S	G	G	G
			442			451			460			469			478			487
	GGT	TCT	CAG	GTC	CAG	CTG	CAG	GAG	TCT	GGA	CCT	GGC	CTG	GTG	GCG	CCC	TCA	CAG
	G	S	Q	V	Q	L	Q	E	S	G	P	G	L	V	A	P	S	Q

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496	505	514	523	532	541
AGC CTG TCC ATC ACA TGC ACC ATC TCA GGG TTC TCA TTA ACT AAG TAT GGT GTA					
S L S I T C T I S G F S L T K Y G V					
550	559	568	577	586	595
CAC TGG GTT CGC CAG CCT CCA GGA AAG GGT CTG GAG TGG CTG GTG GTG ATA TGG					
H W V R Q P P G K G L E W L V V I W					
604	613	622	631	640	649
ACT GAT GGA GGC ACA TCC TAT AAT TCA GCT CTC AAA TCC AGA CTG AGC ATC ACC					
T D G G T S Y N S A L K S R L S I S					
658	667	676	685	694	703
AAG GAC AAC TCC AAG AGC CAA GTT TTC TTA AAA ATG AAC AGT CTC CAA ACT GAT					
K D N S K S Q V F L K M N S L Q T D					
712	721	730	739	748	757
GAC ACA GCC ATG TAC TAC TGT GCC AGA CAG GAT AGA TAC GAC GGT GGA ATT GCT					
D T A M Y Y C A R Q D R Y D G G I A					
766	775	784	<u>BspEI</u>		
TAC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCC GGA 3'					
Y W G Q G T T V T V S S					

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Figure 7

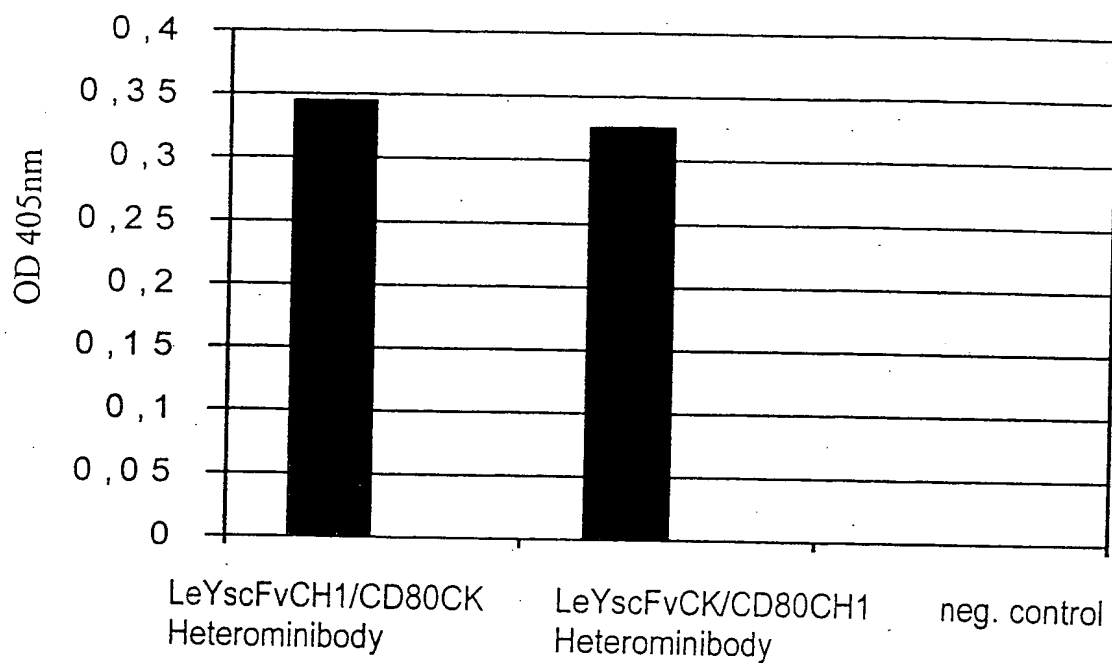
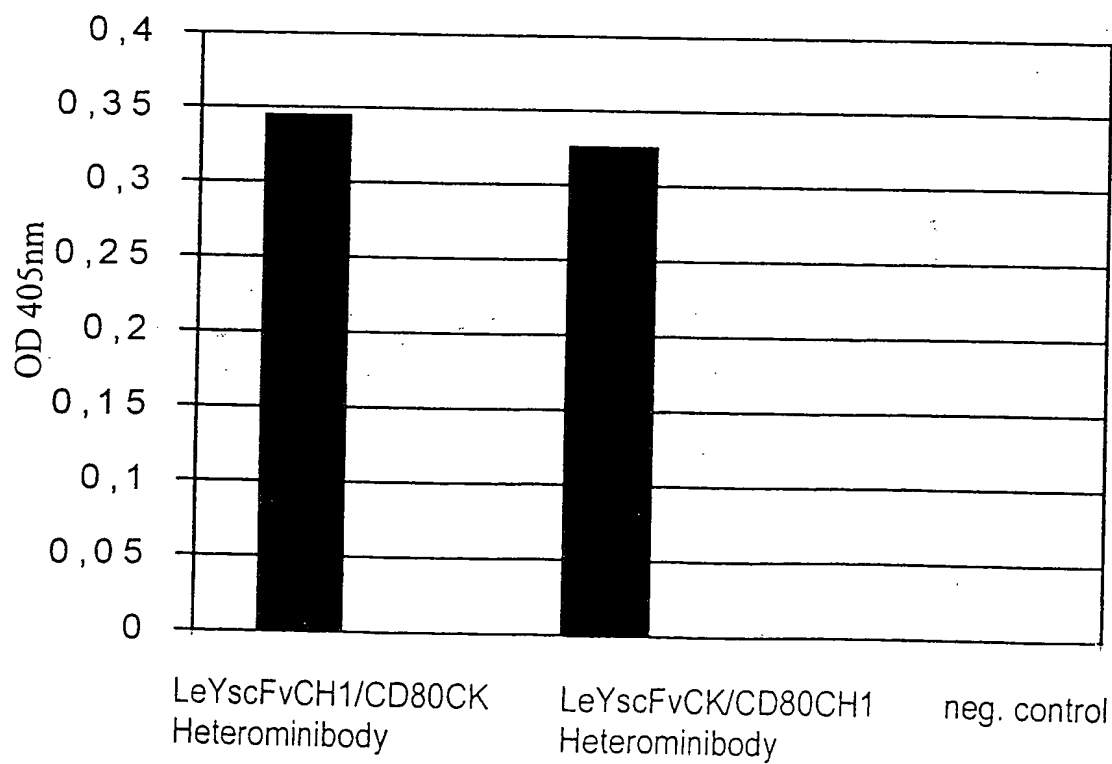
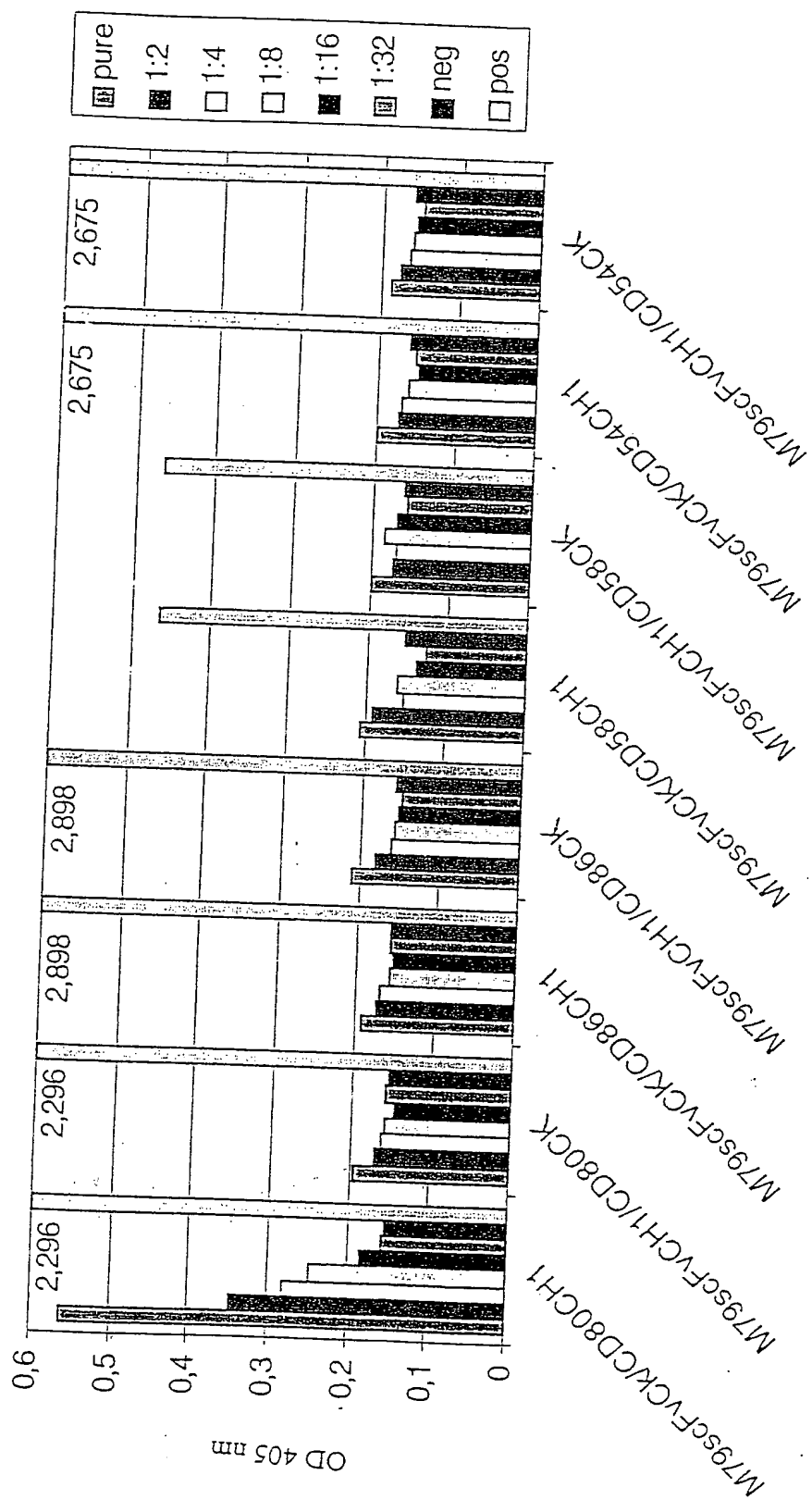


Figure 8





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Figure 10

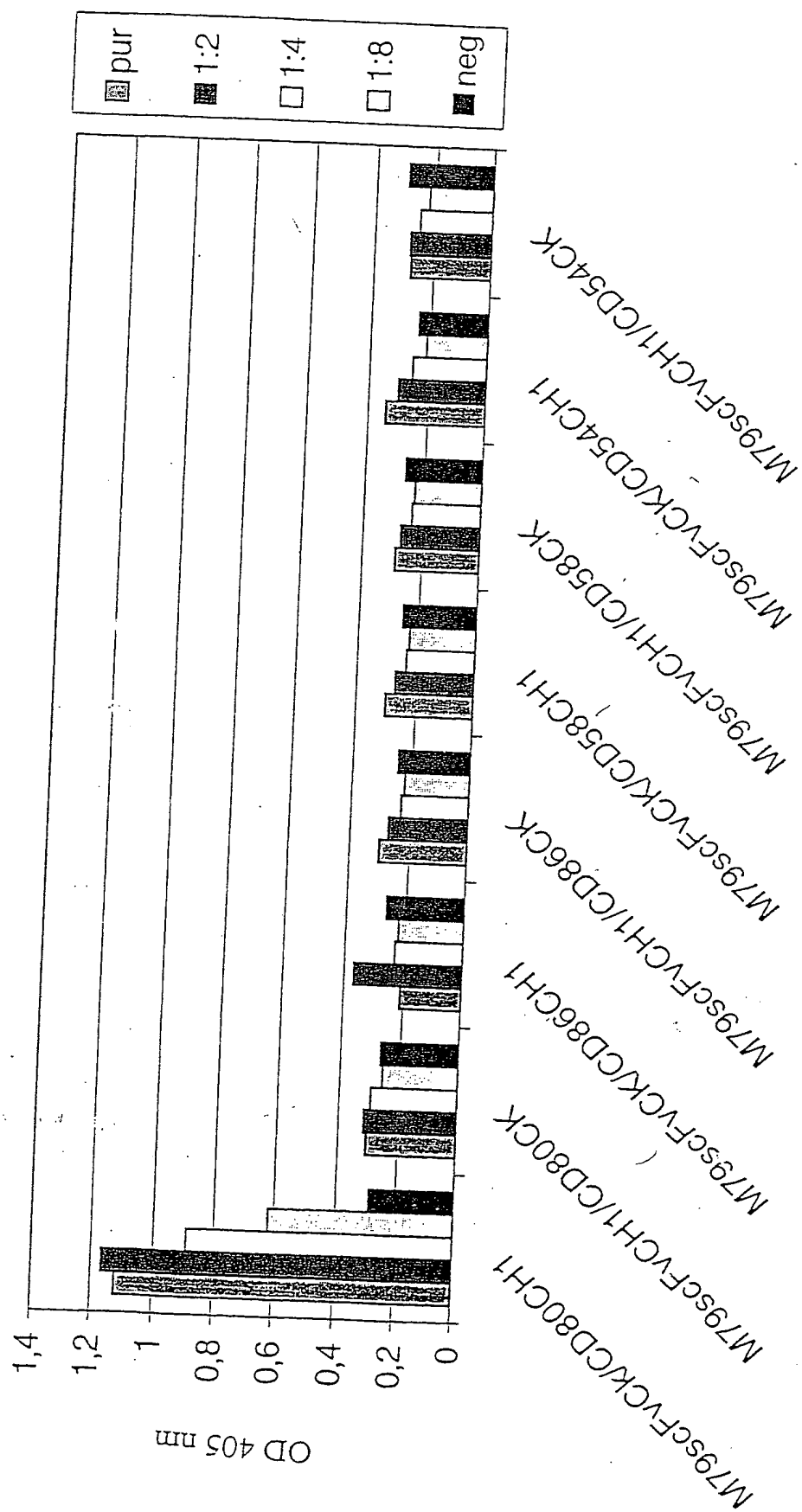
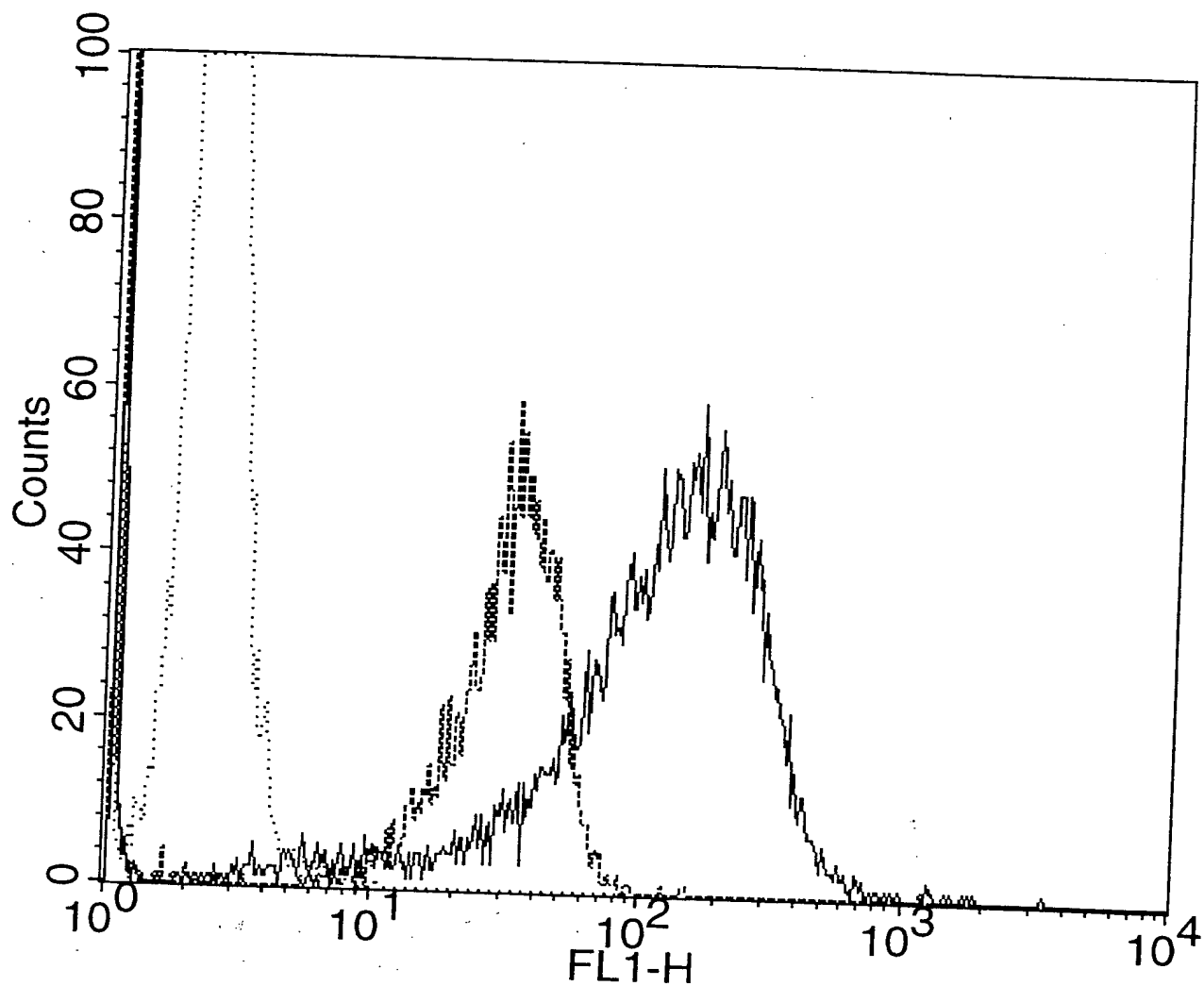
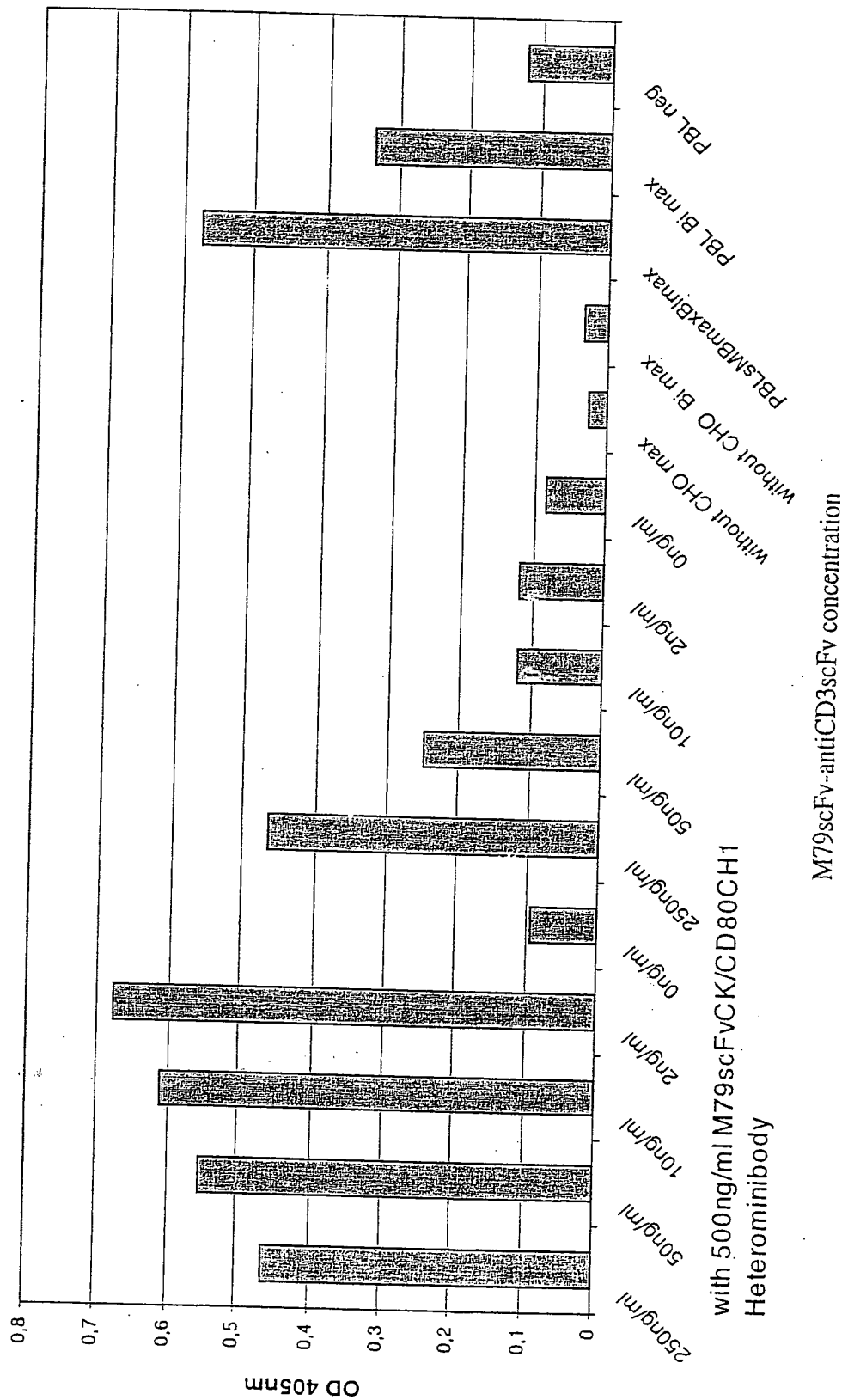


Figure 11



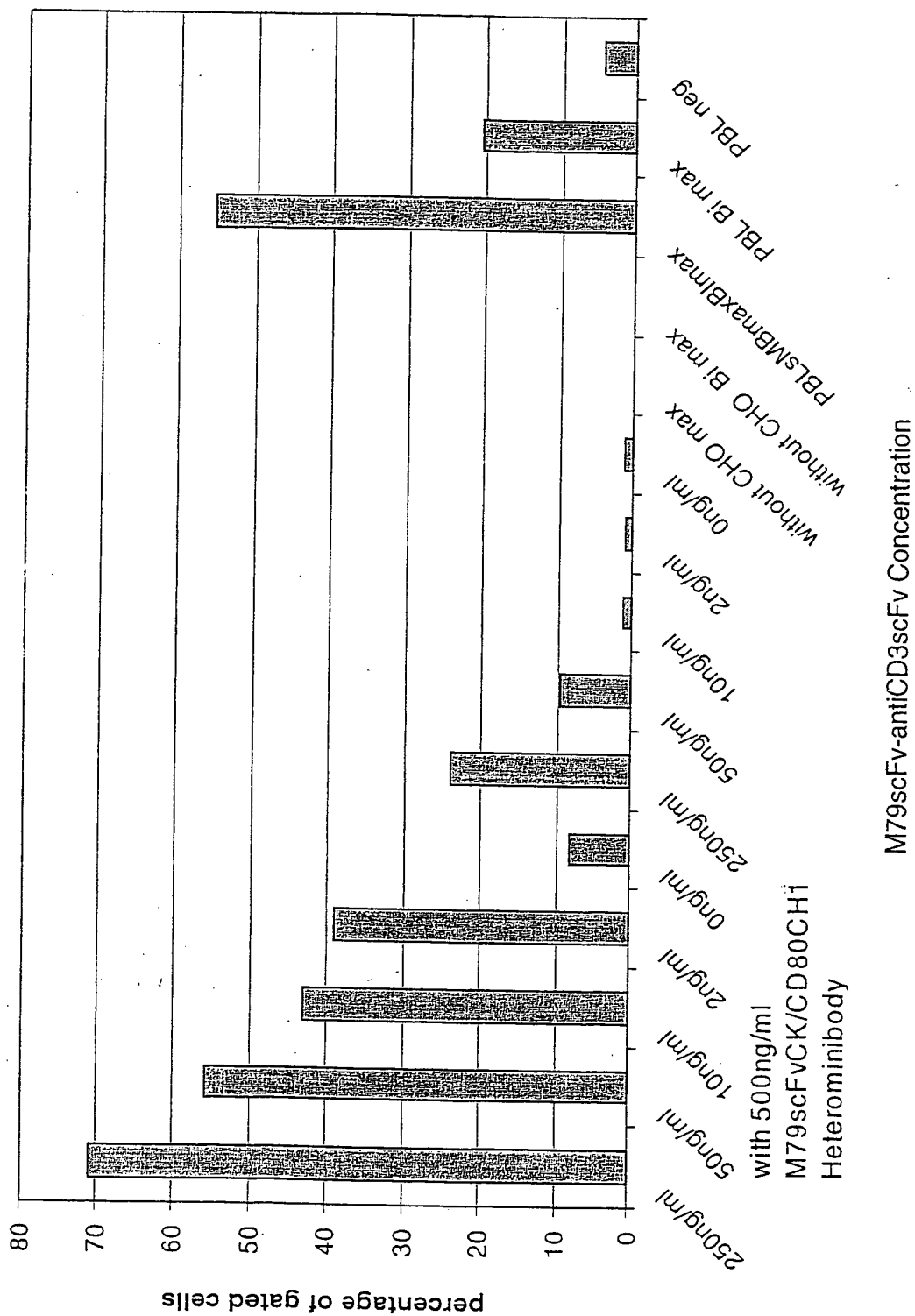
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Figure 12



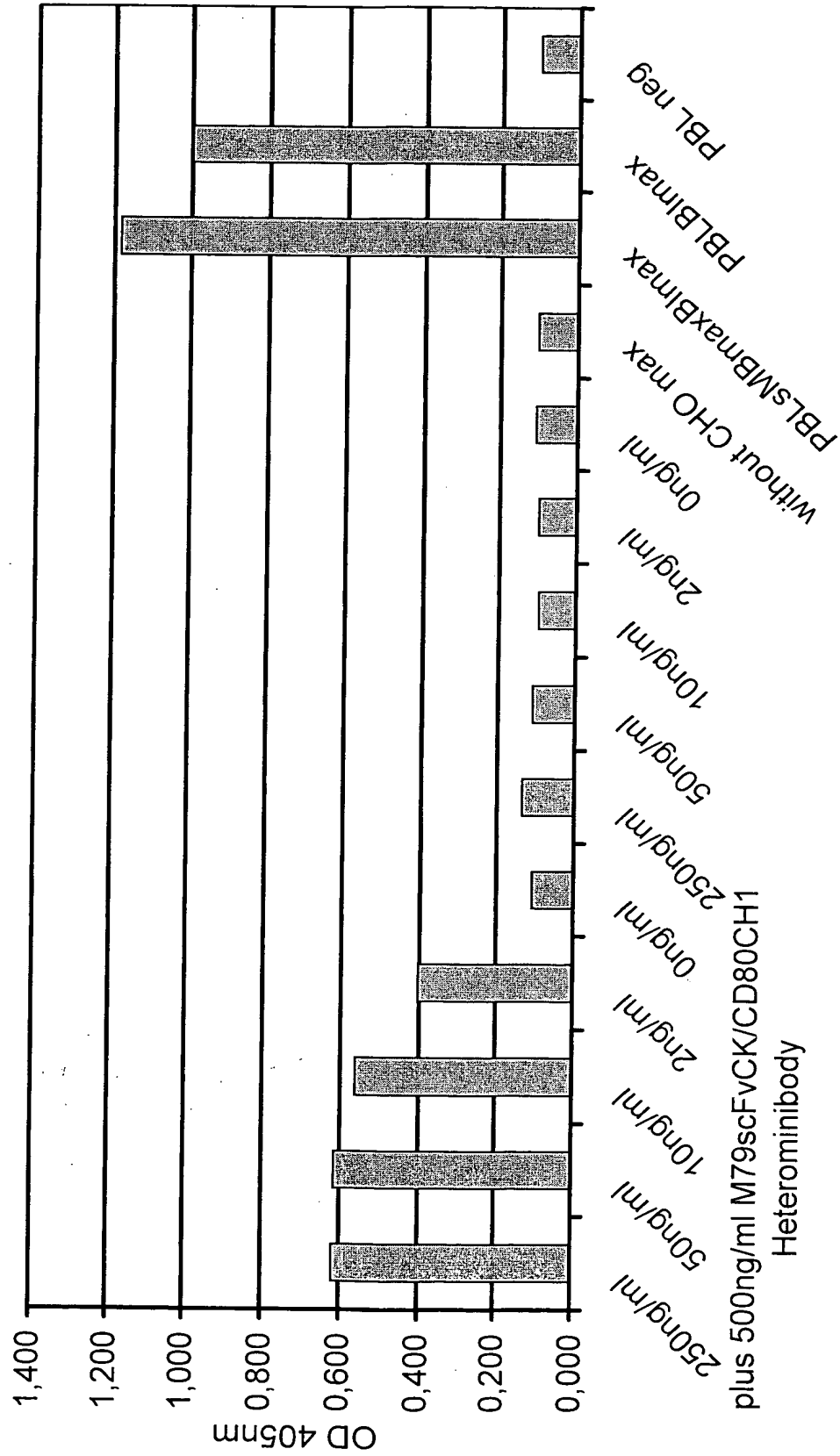
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Figure 14



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Figure 15



M79scFv-anti-CD3scFv Concentration

Figure 16

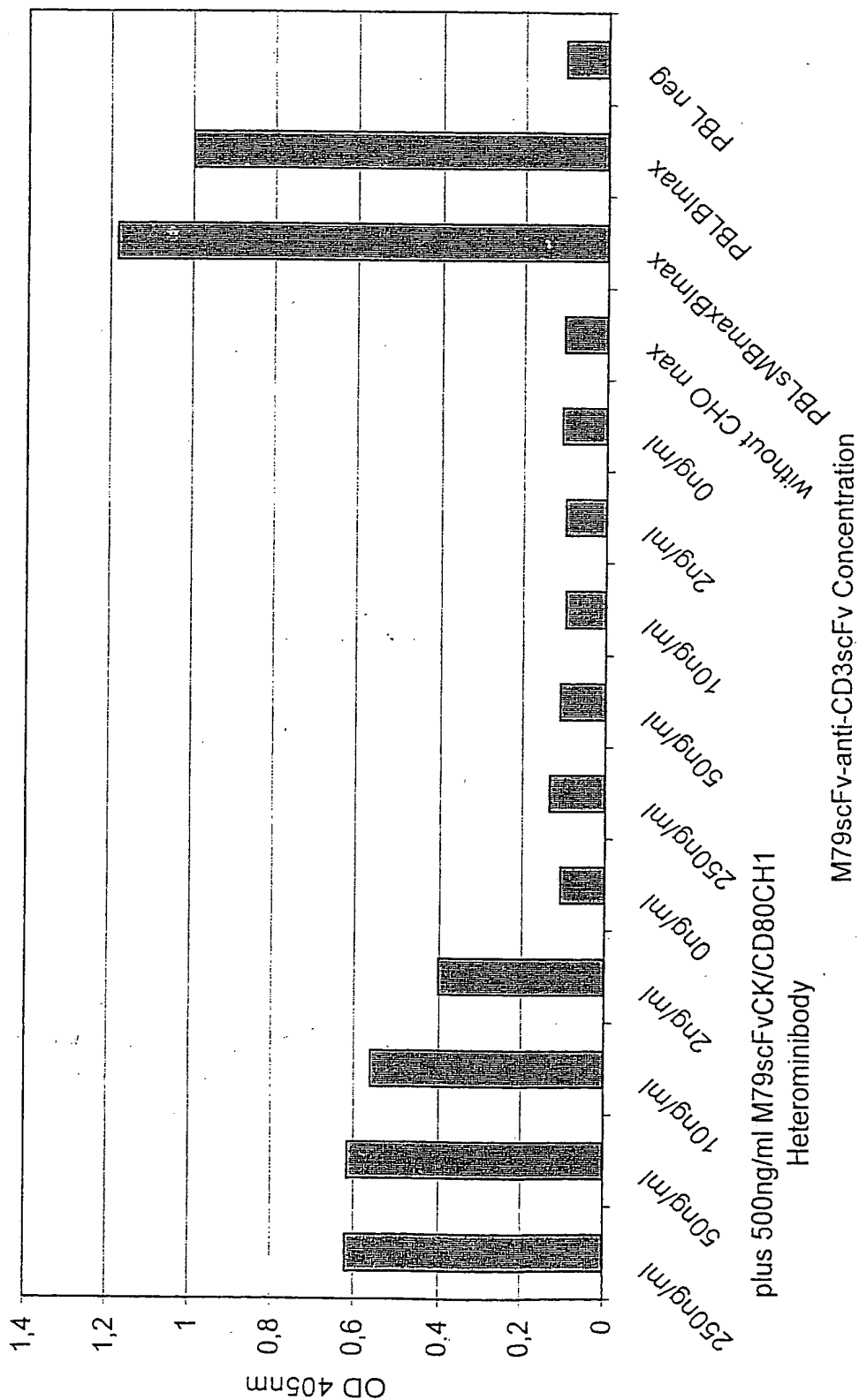


Figure17

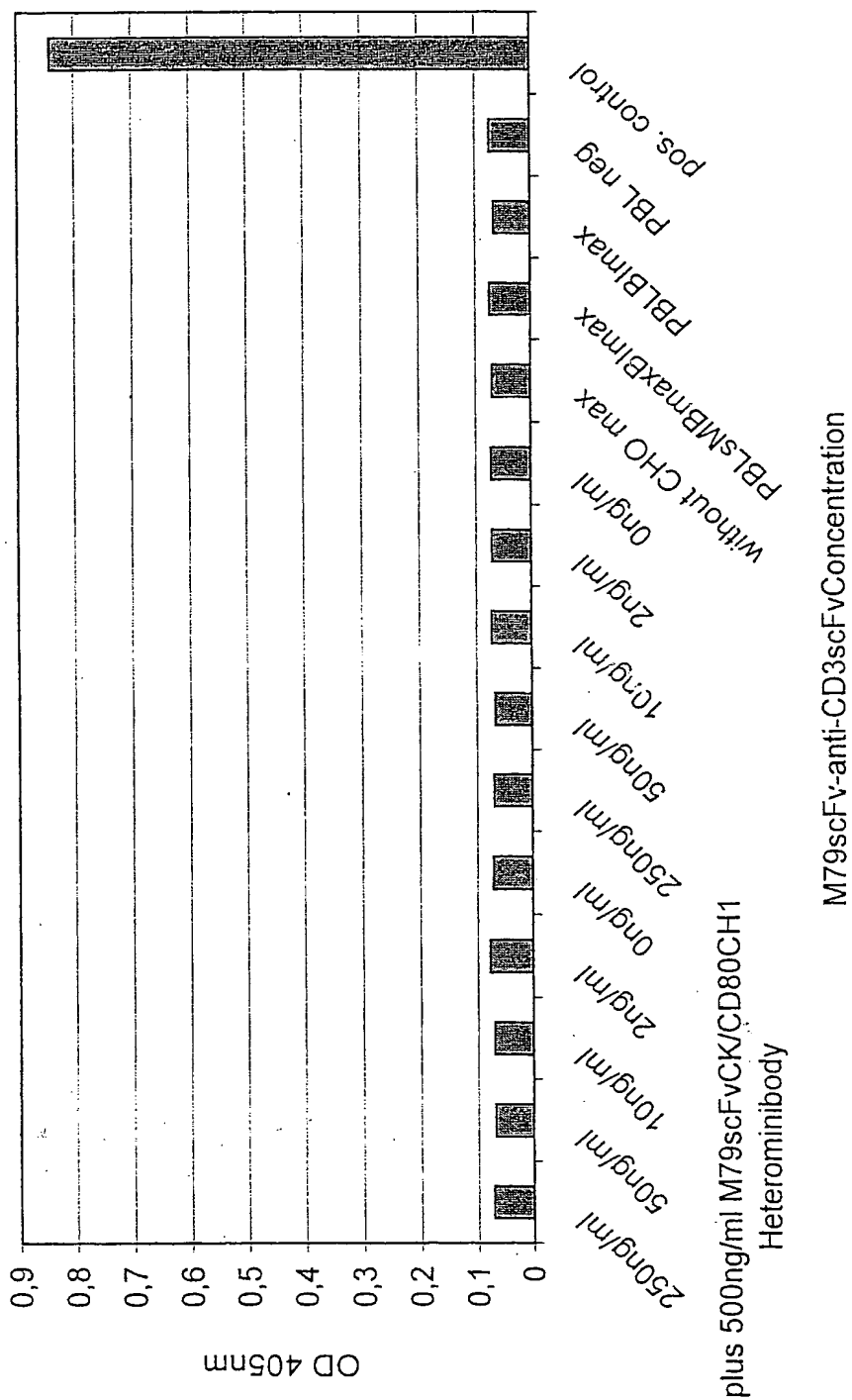
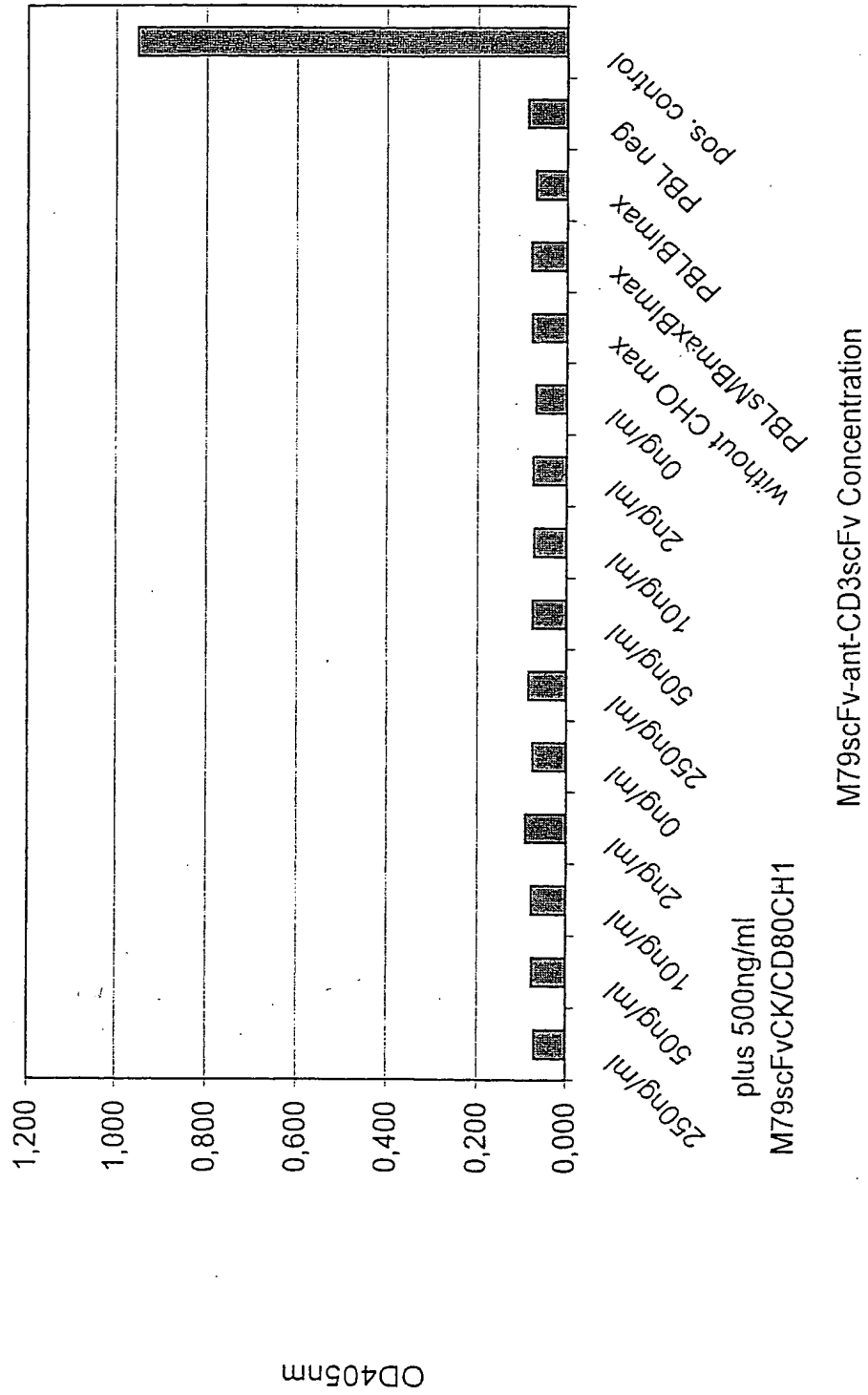
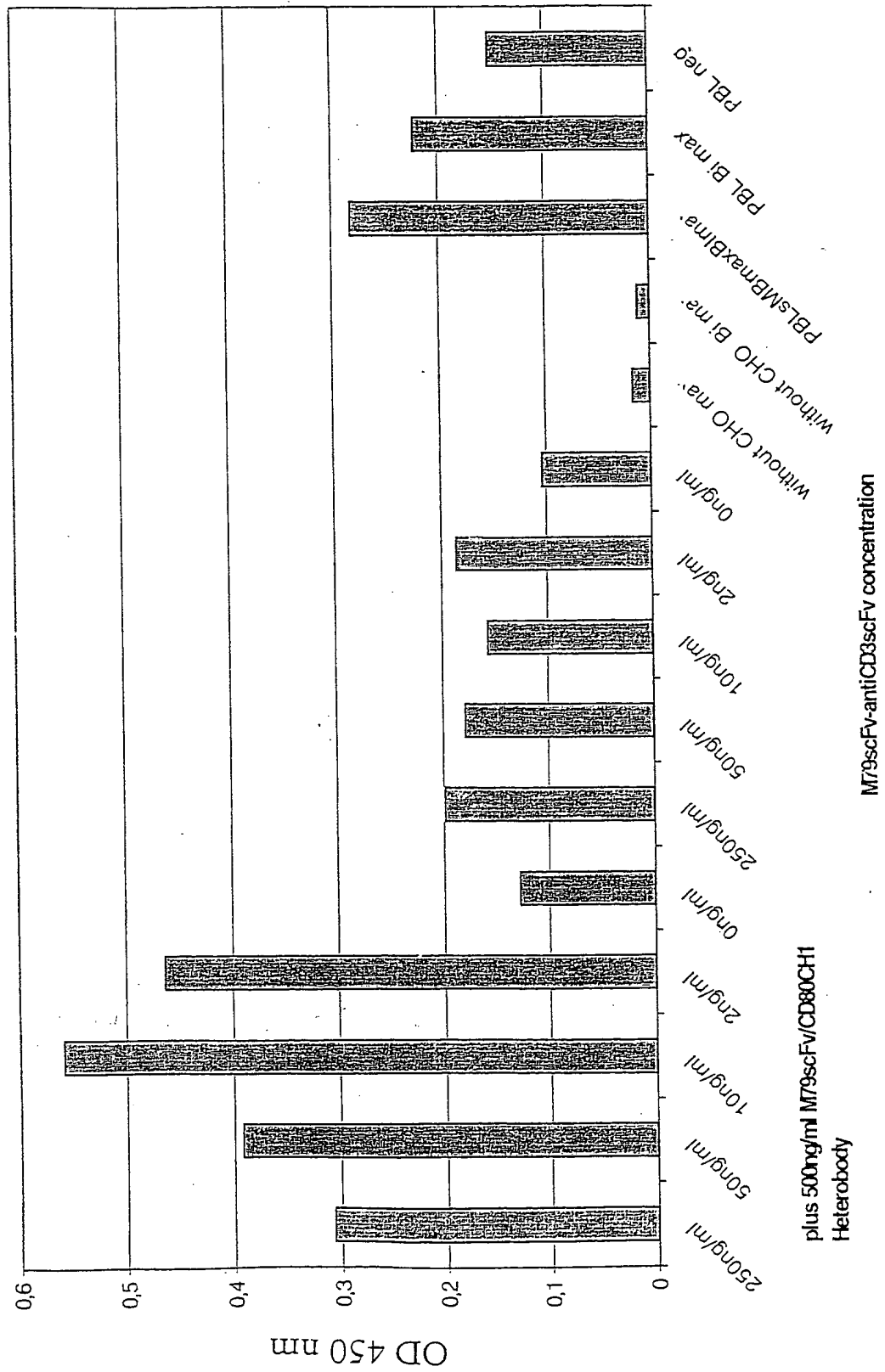


Figure18



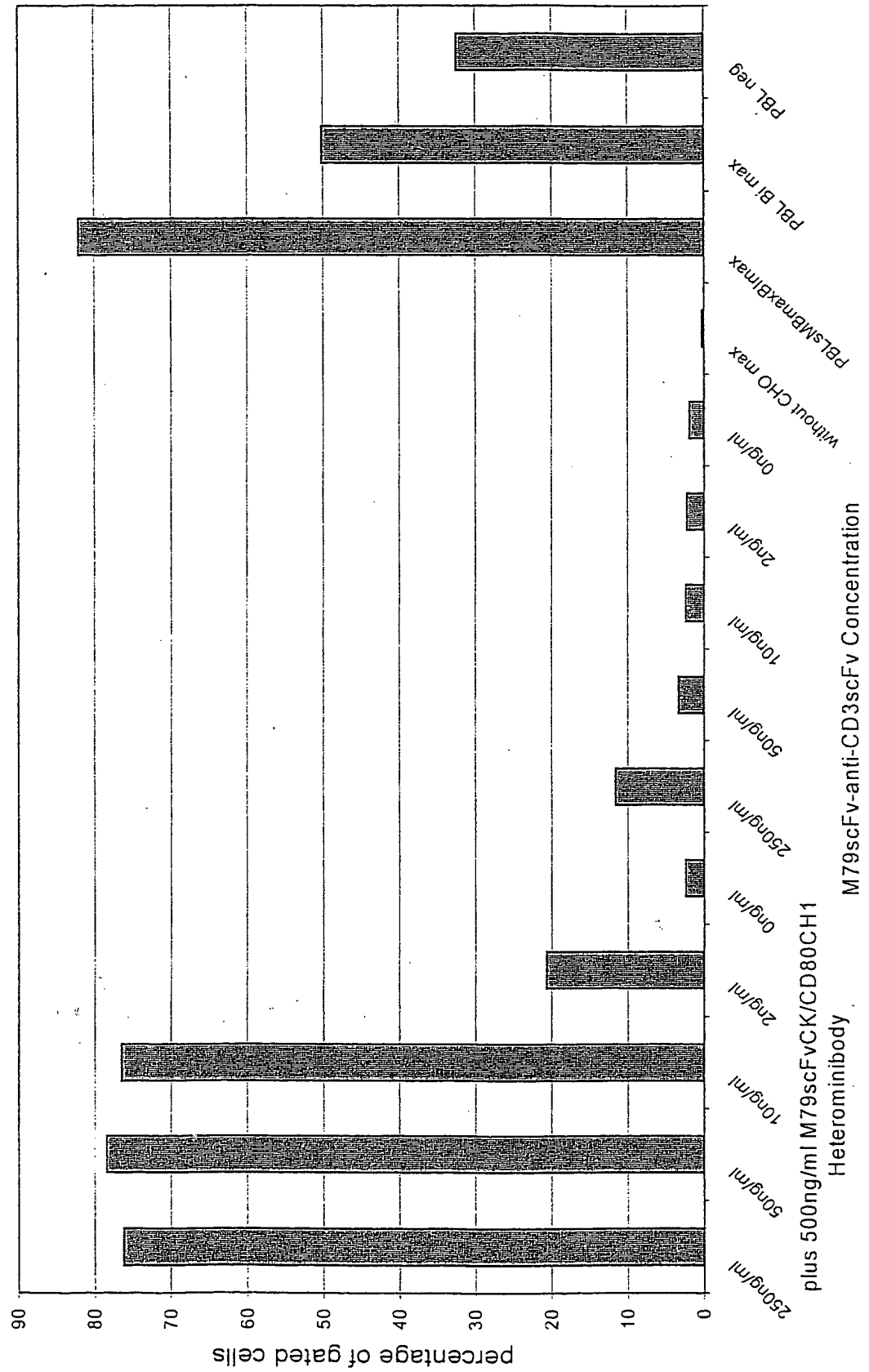
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Figure 19



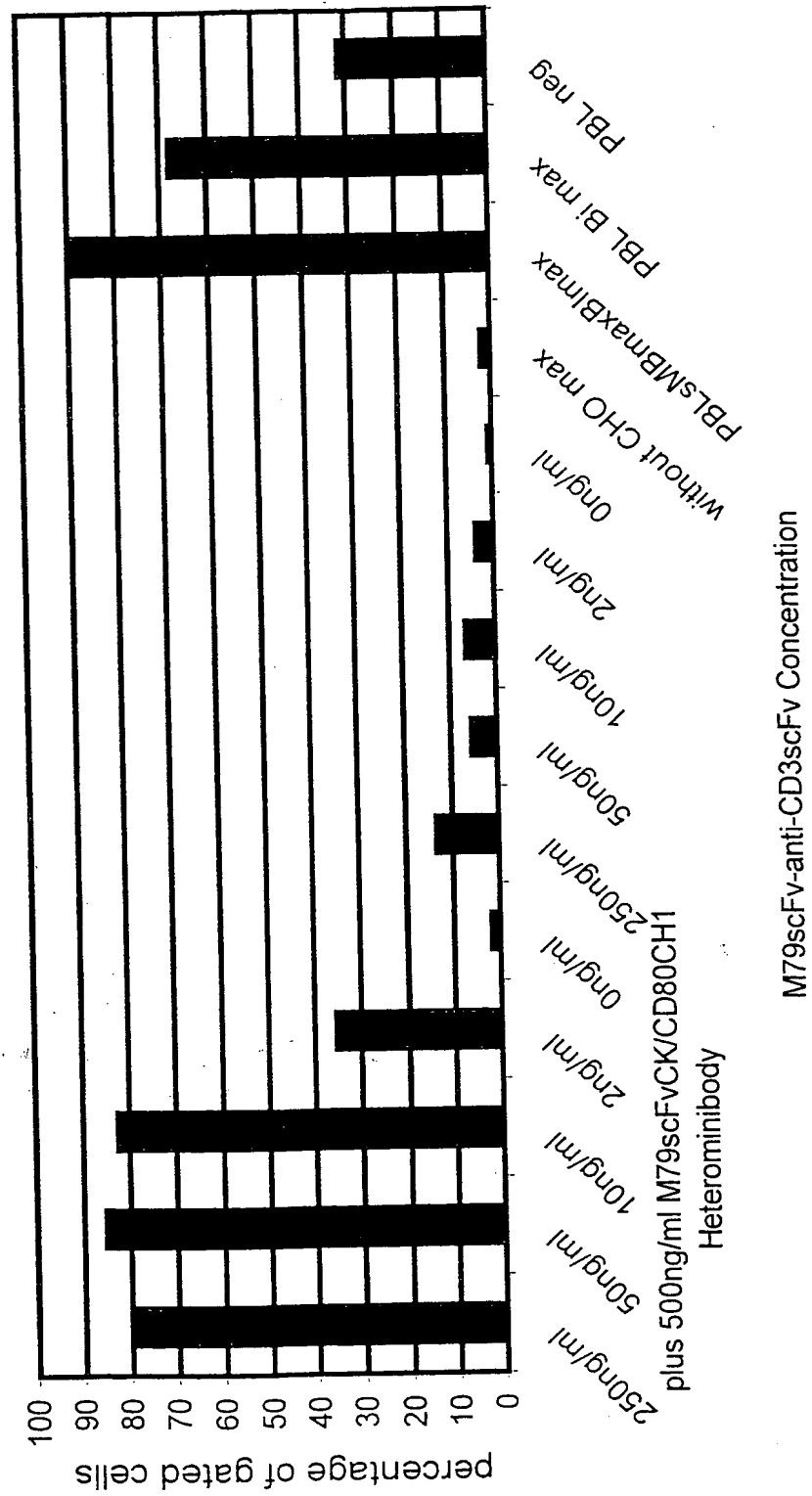
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Figure 20

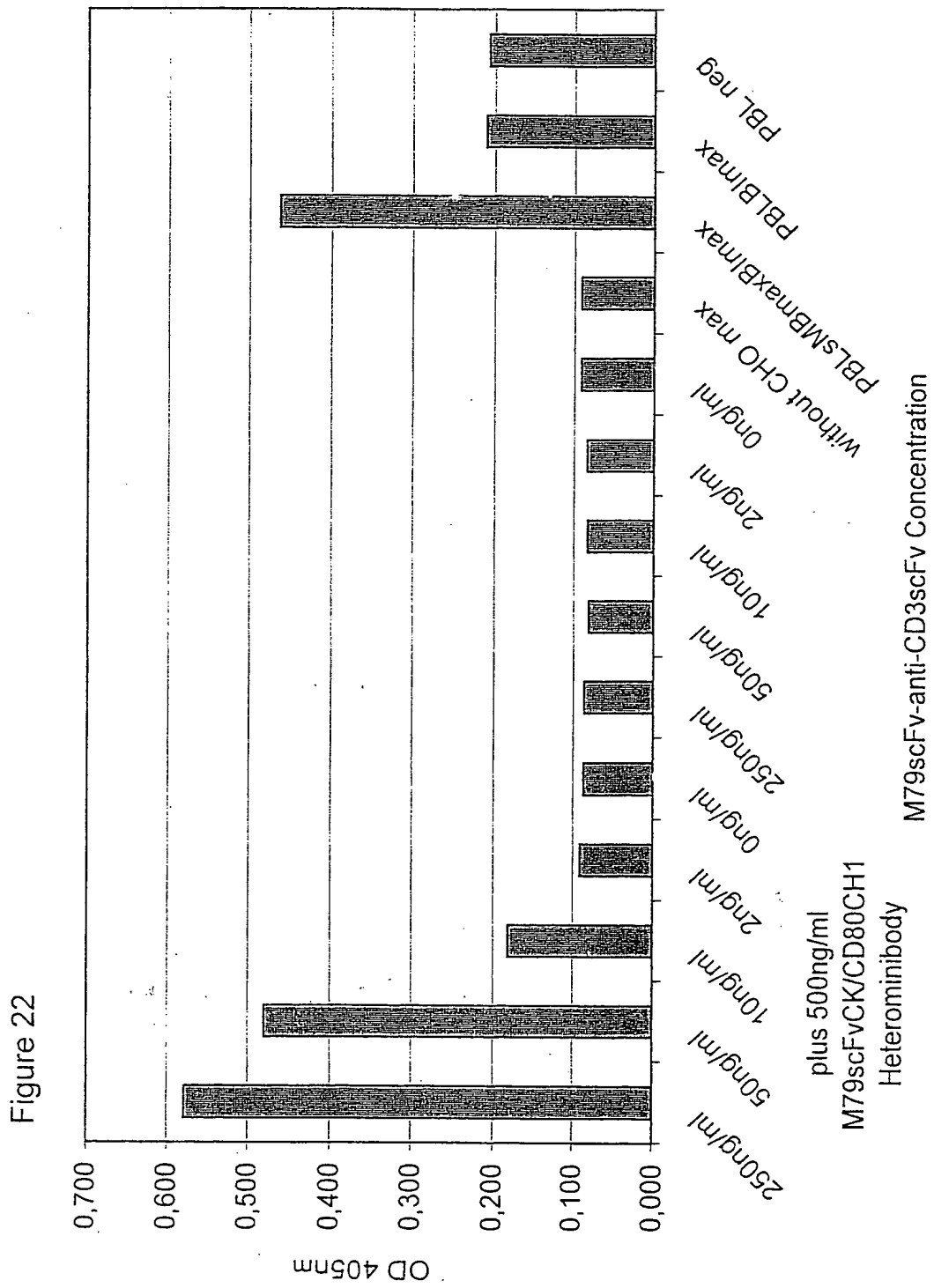


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Figure 21

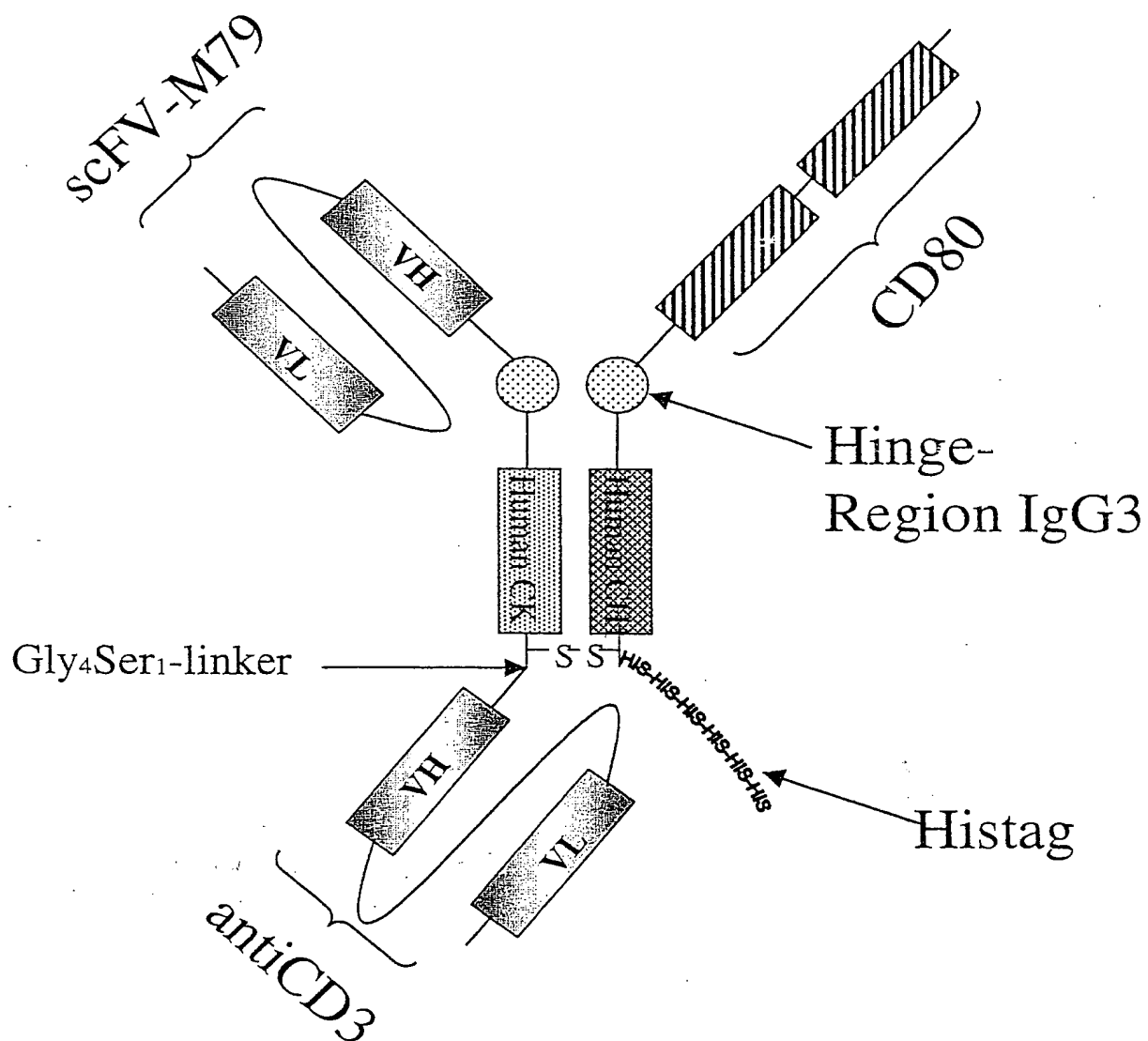


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Figure 23



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Figure 24

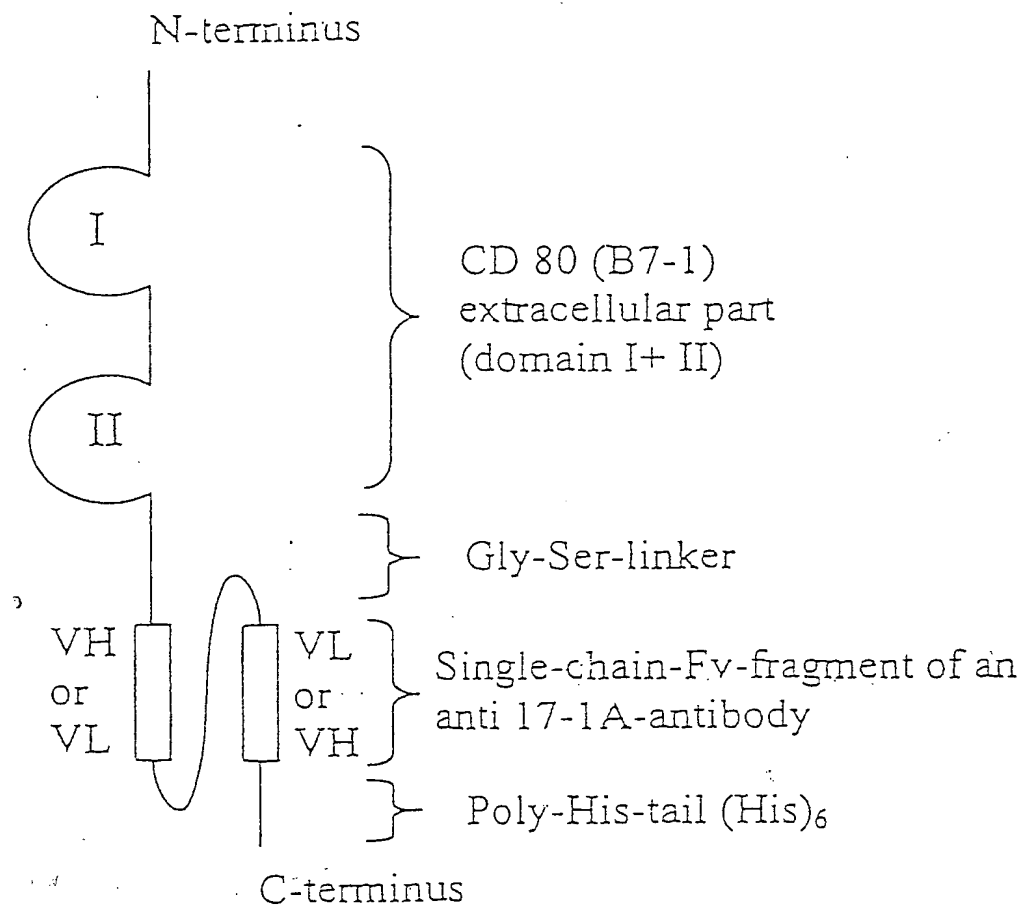
Recombinant bifunctional single-chain protein

Figure 25

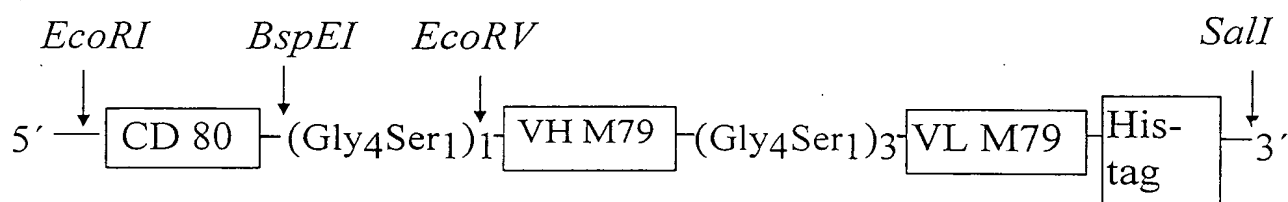
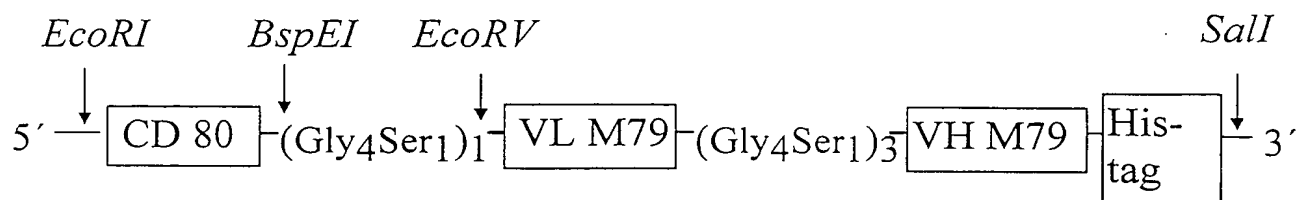


Figure 26

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ELISA-analysis
CD80-M79scFv (VL/VH) with short linker
Detection: anti-His-tag

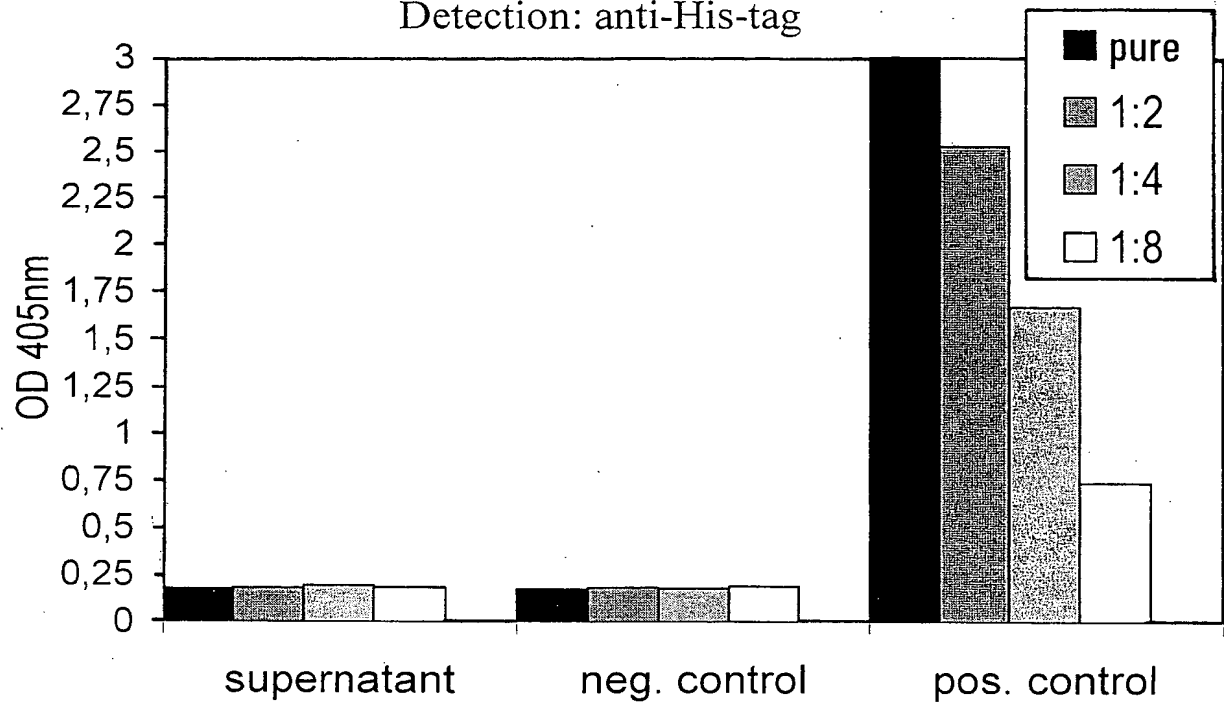
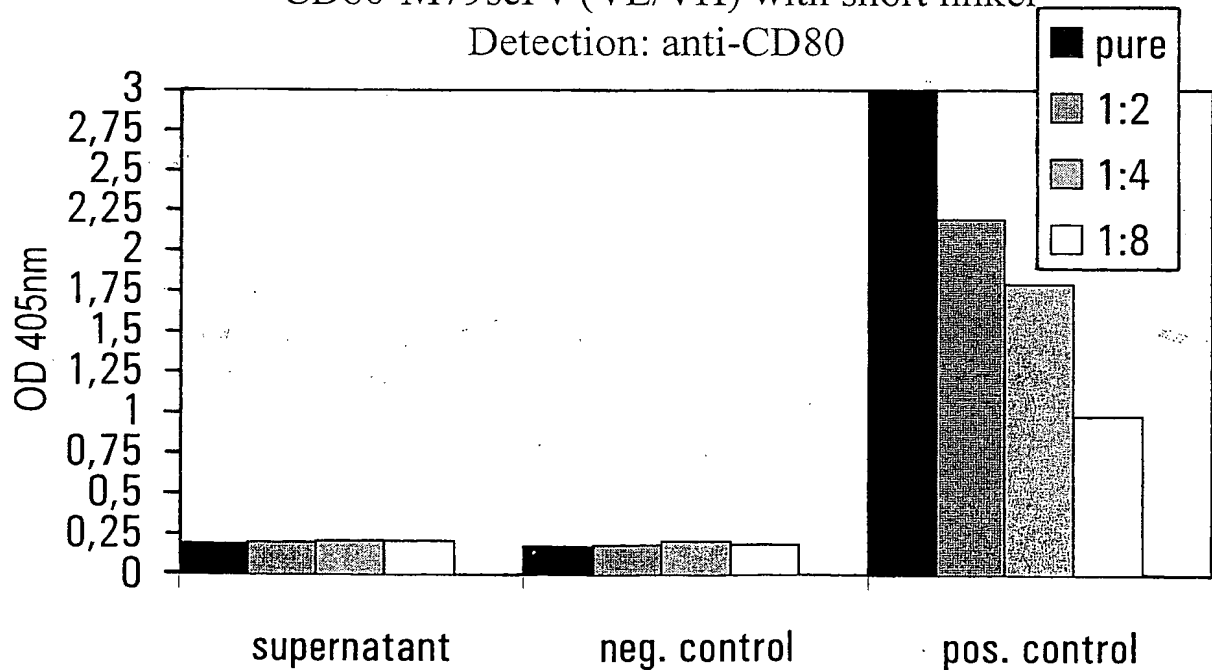


Figure 27

ELISA-analysis
CD80-M79scFv (VL/VH) with short linker
Detection: anti-CD80



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Figure 28

ELISA-analysis

CD80-M79scFv (VL/VH) with short linker

Detection: anti-His-tag or anti-CD80 (as indicated)

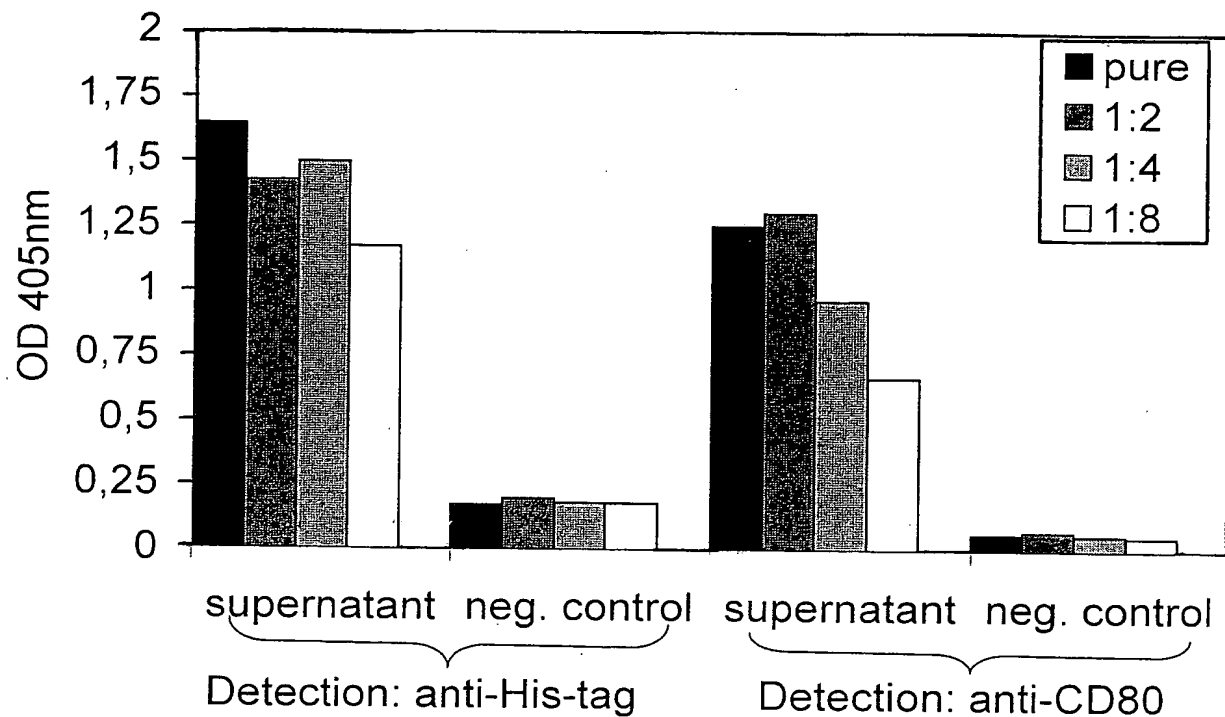


Figure 29

ELISA-analysis

CD80-M79 scFv (VH/VL) with short linker

Detection: anti-CD80

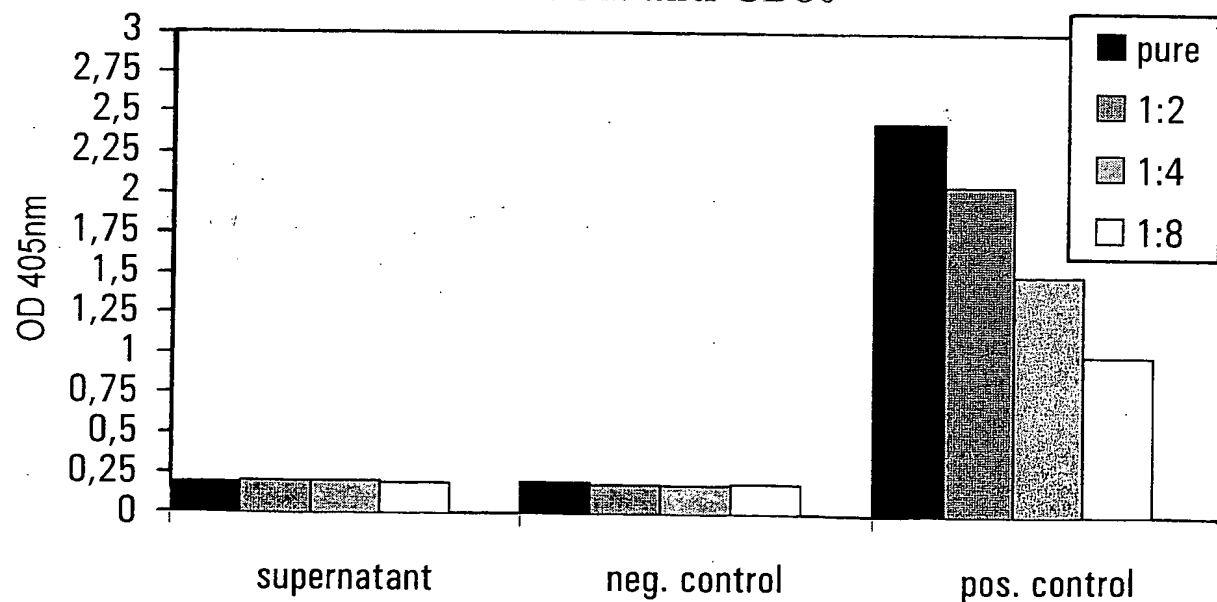
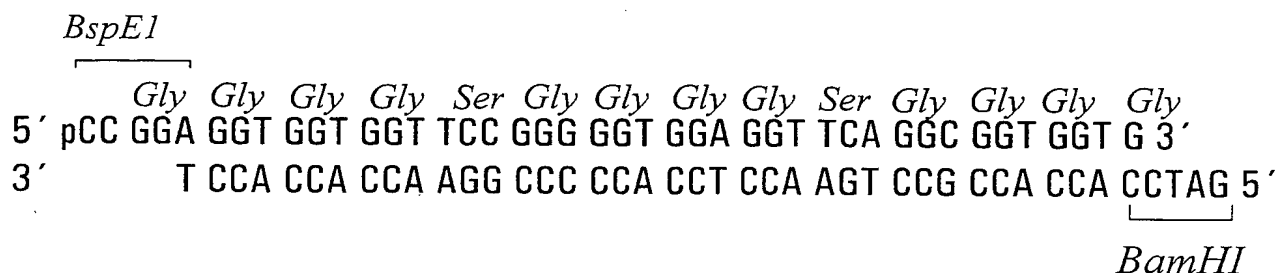


Figure 30

DNA-sequence of the double-stranded oligonucleotide designated ACCGS15 BAM

**Figure 31**

ELISA-analysis
CD80-M79scFv (VH/VL) with long linker
Detection: anti-His-tag

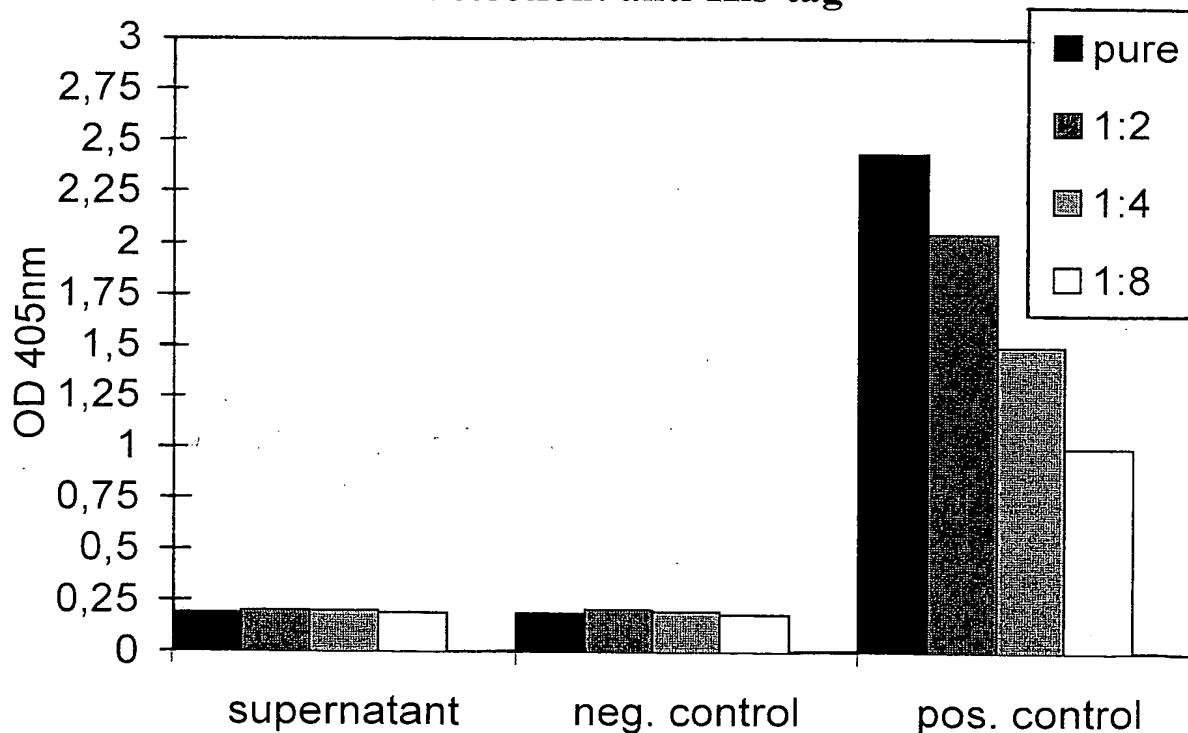


Figure 32

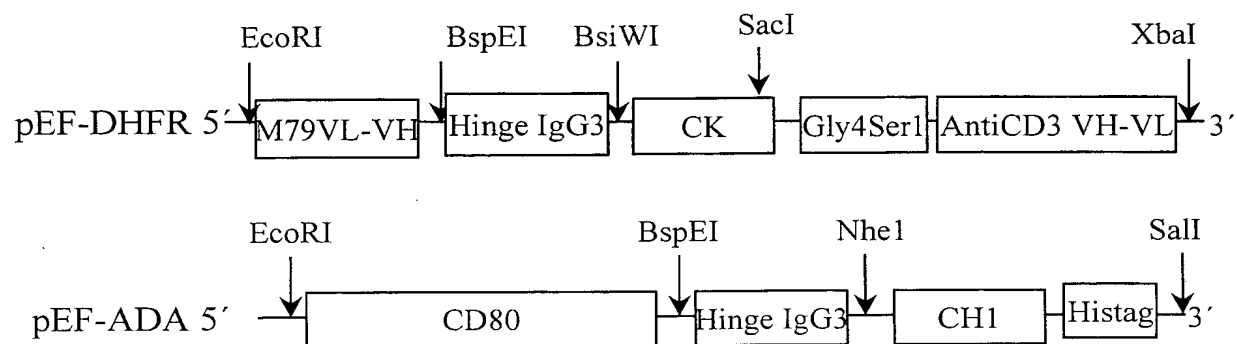
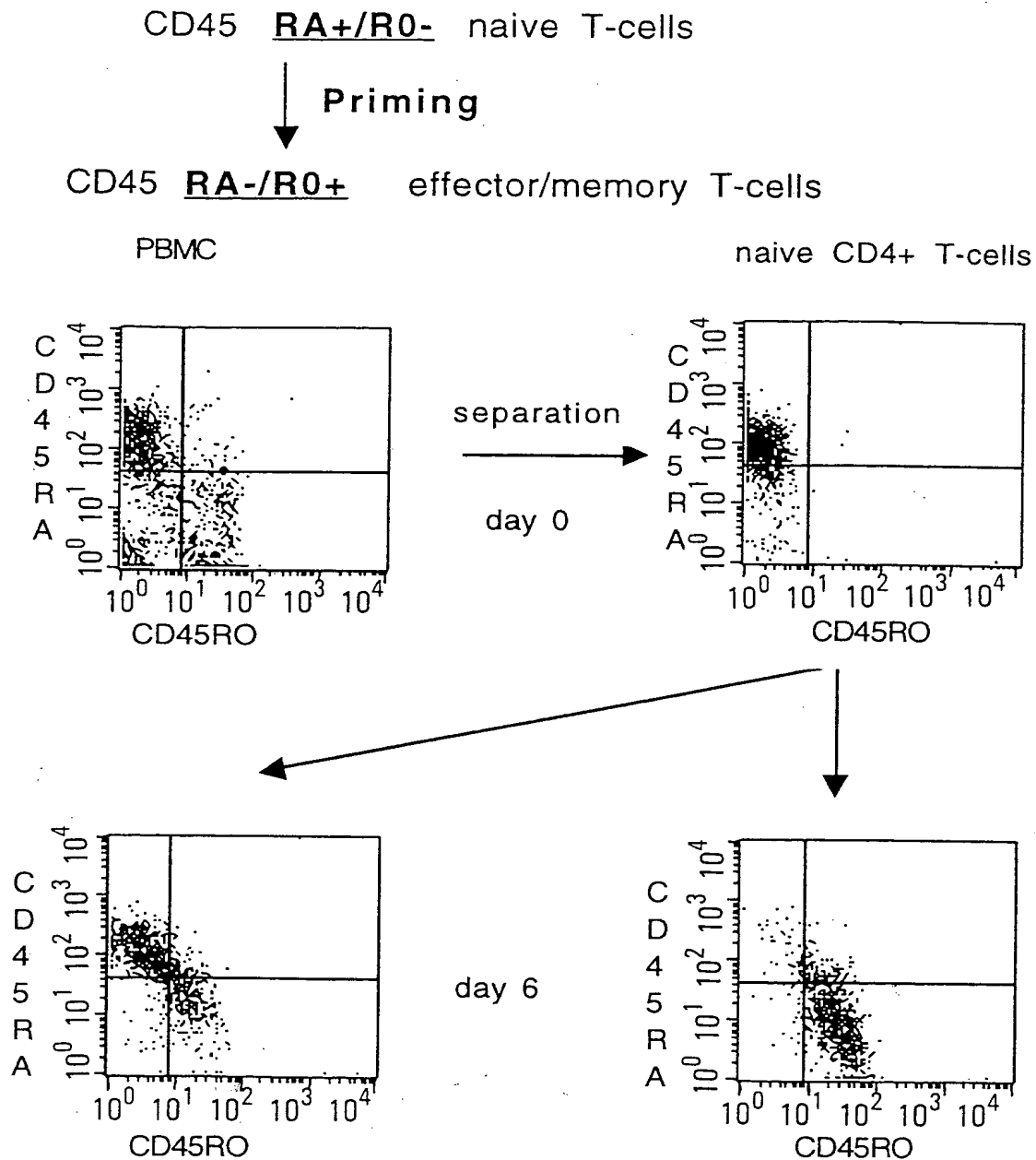


Figure 33 Phenotyp-Switch

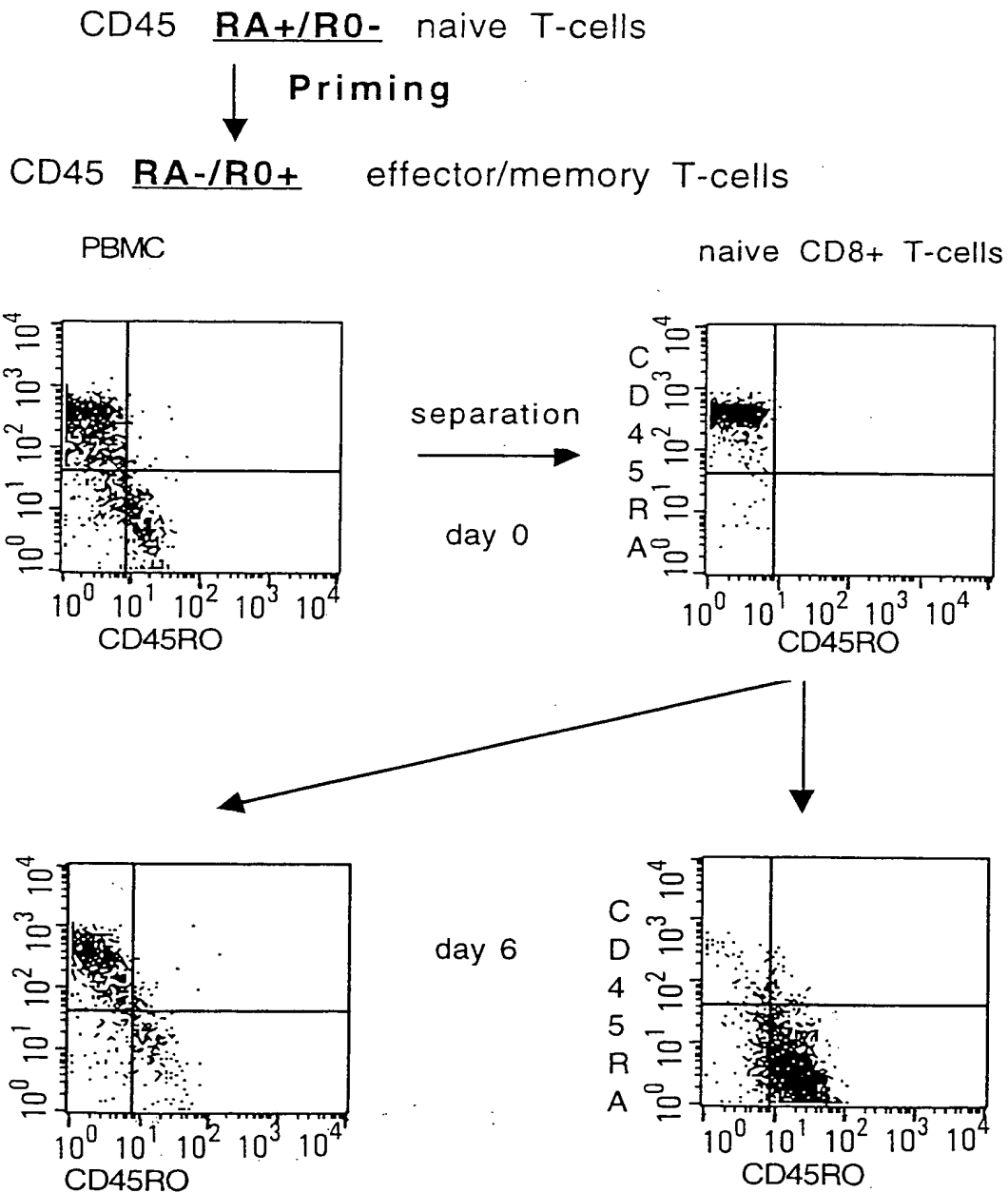


only primary signal:
M79scFv-antiCD3scFv

primary + costimulatory signal:
M79scFv-antiCD3scFv and
M79scFvCK/CD80CH1
Heterominibody

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Figure 34 Phenotyp-Switch

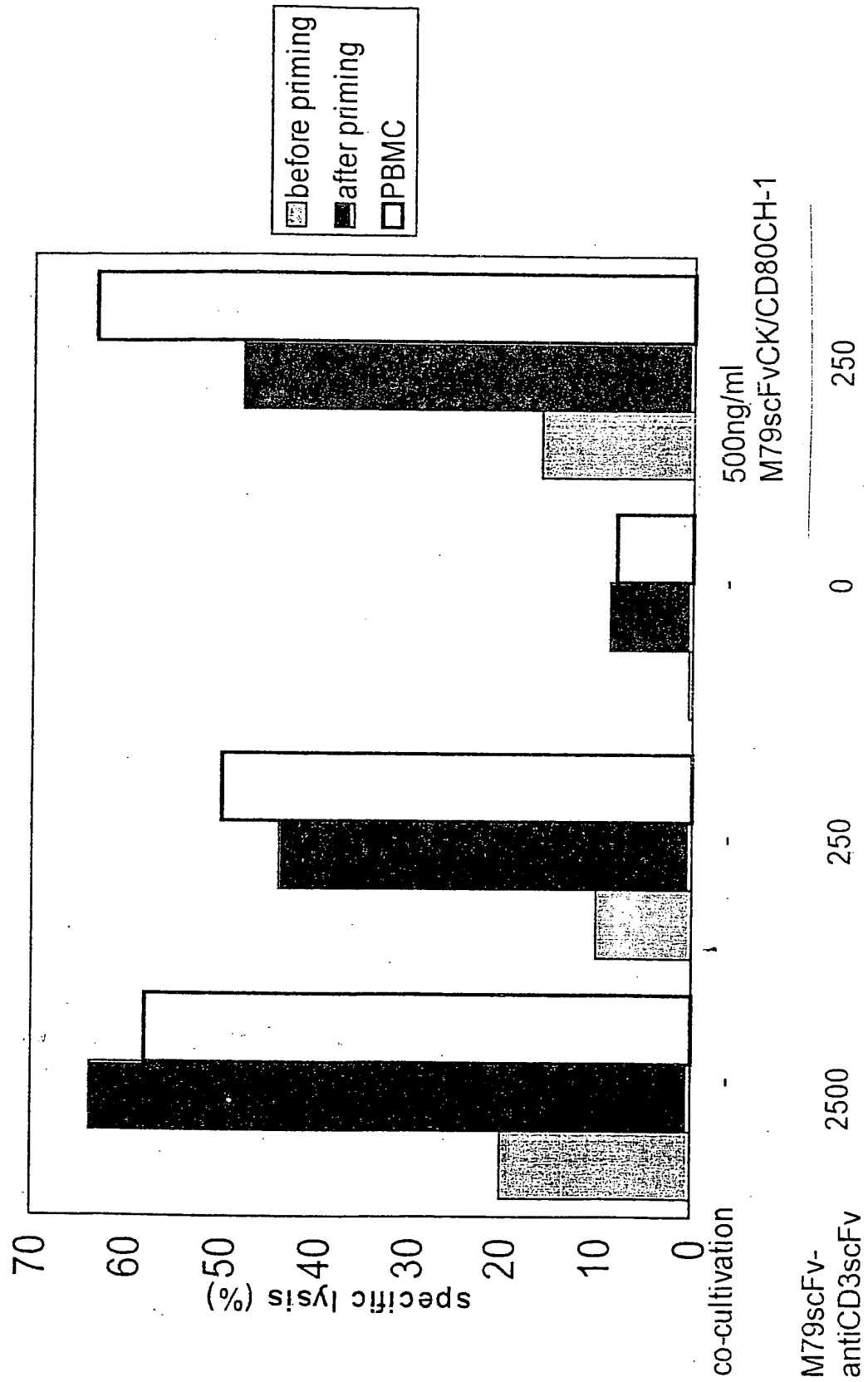


only primary signal:
M79scFv-antiCD3scFv

primary + costimulatory signal:
M79scFv-antiCD3scFv and
M79scFvCK/CD80CH1
Heterominibody

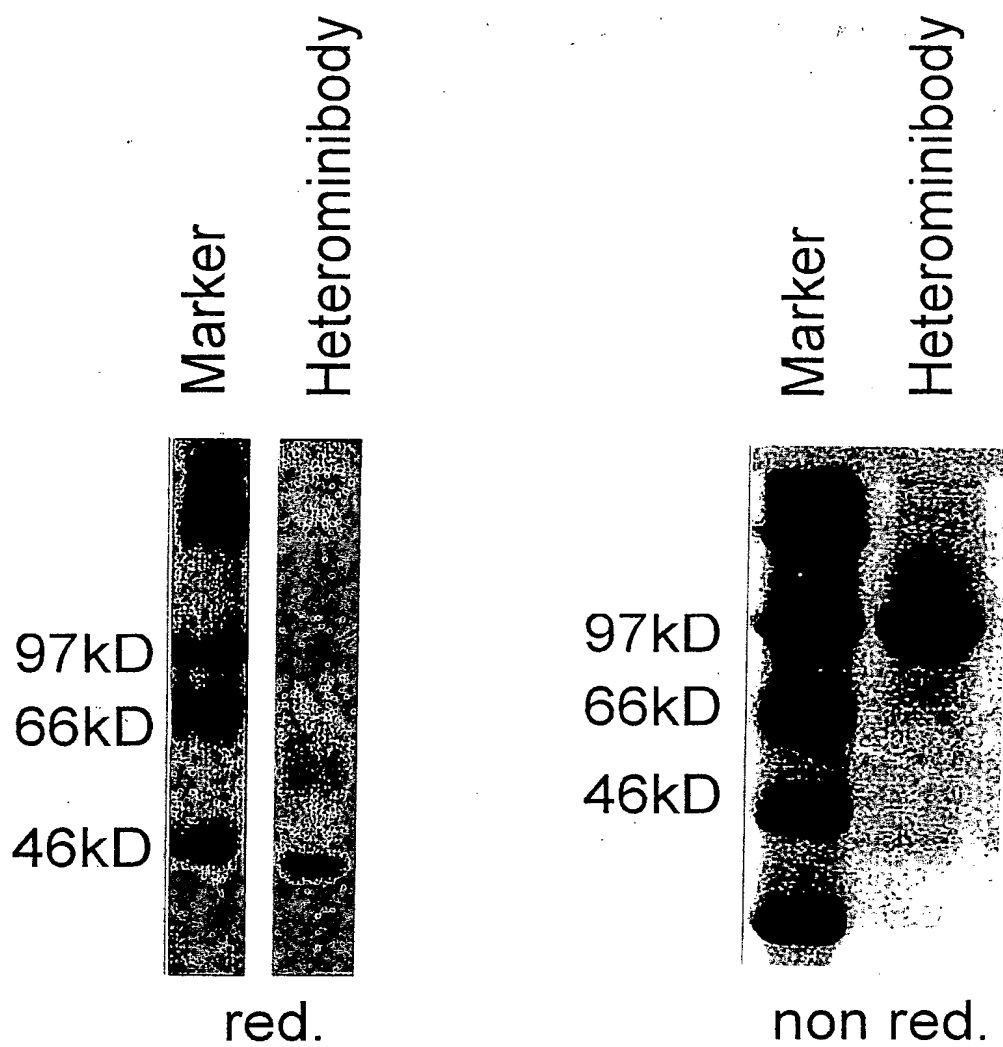
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Figure35



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Figure 36



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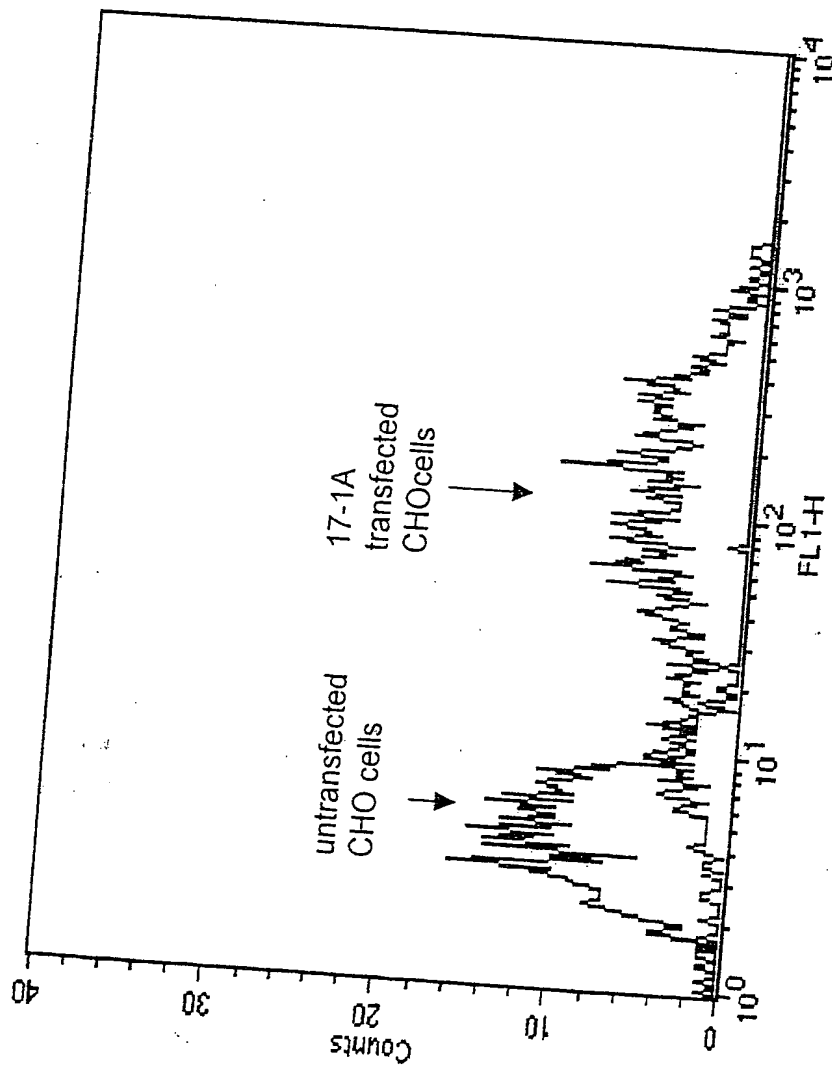


Figure 37

T09120-52944260

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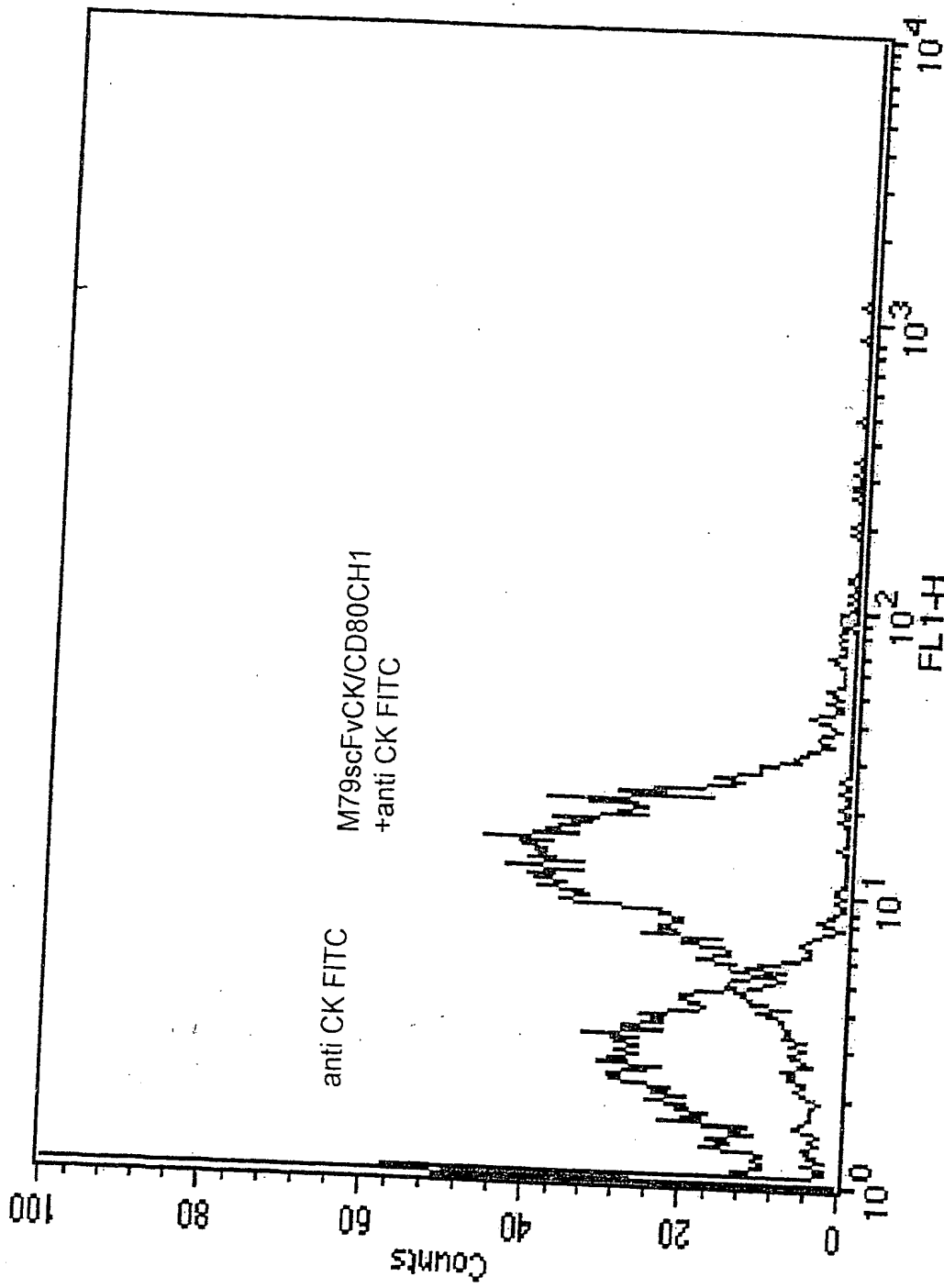


Figure 38

Figure 39

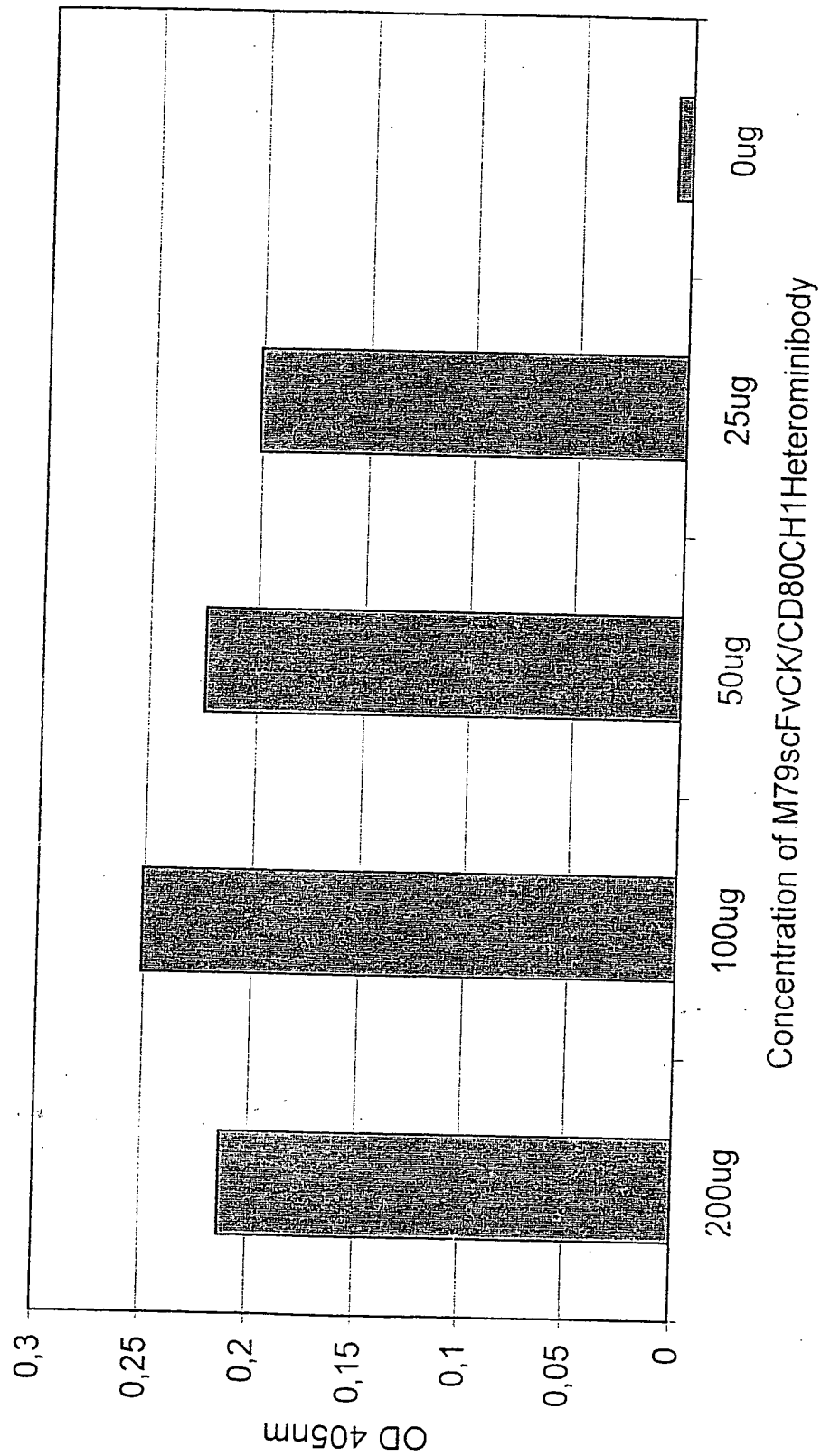


Figure 40

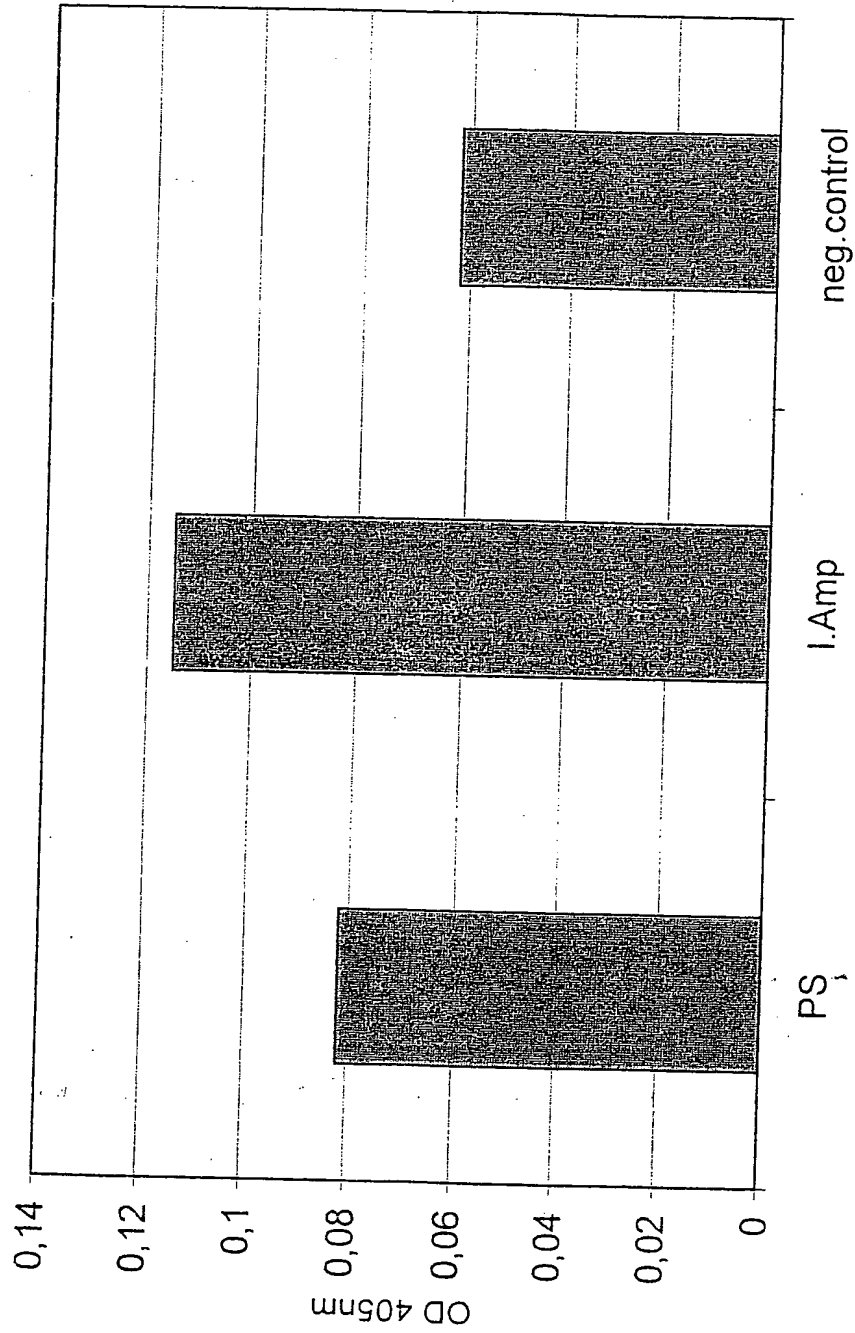


Figure 41

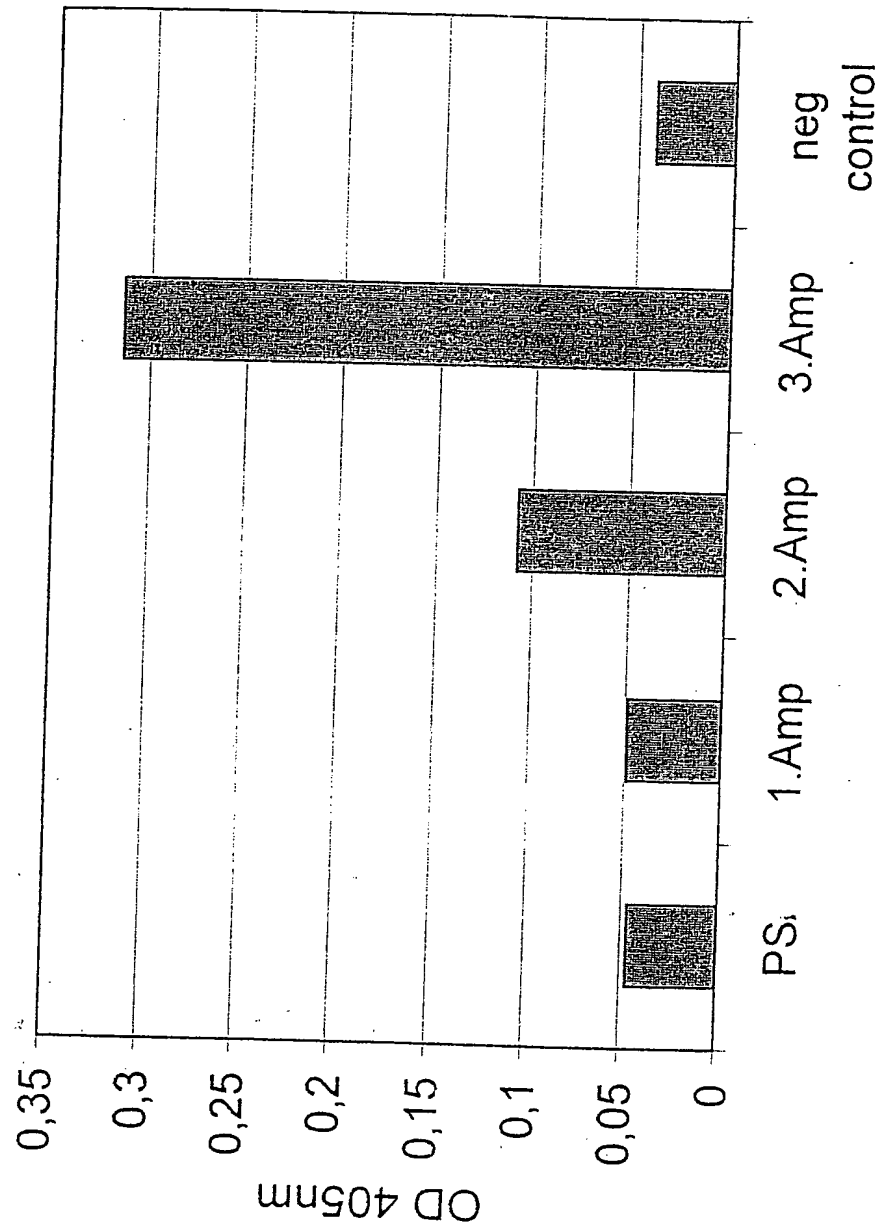
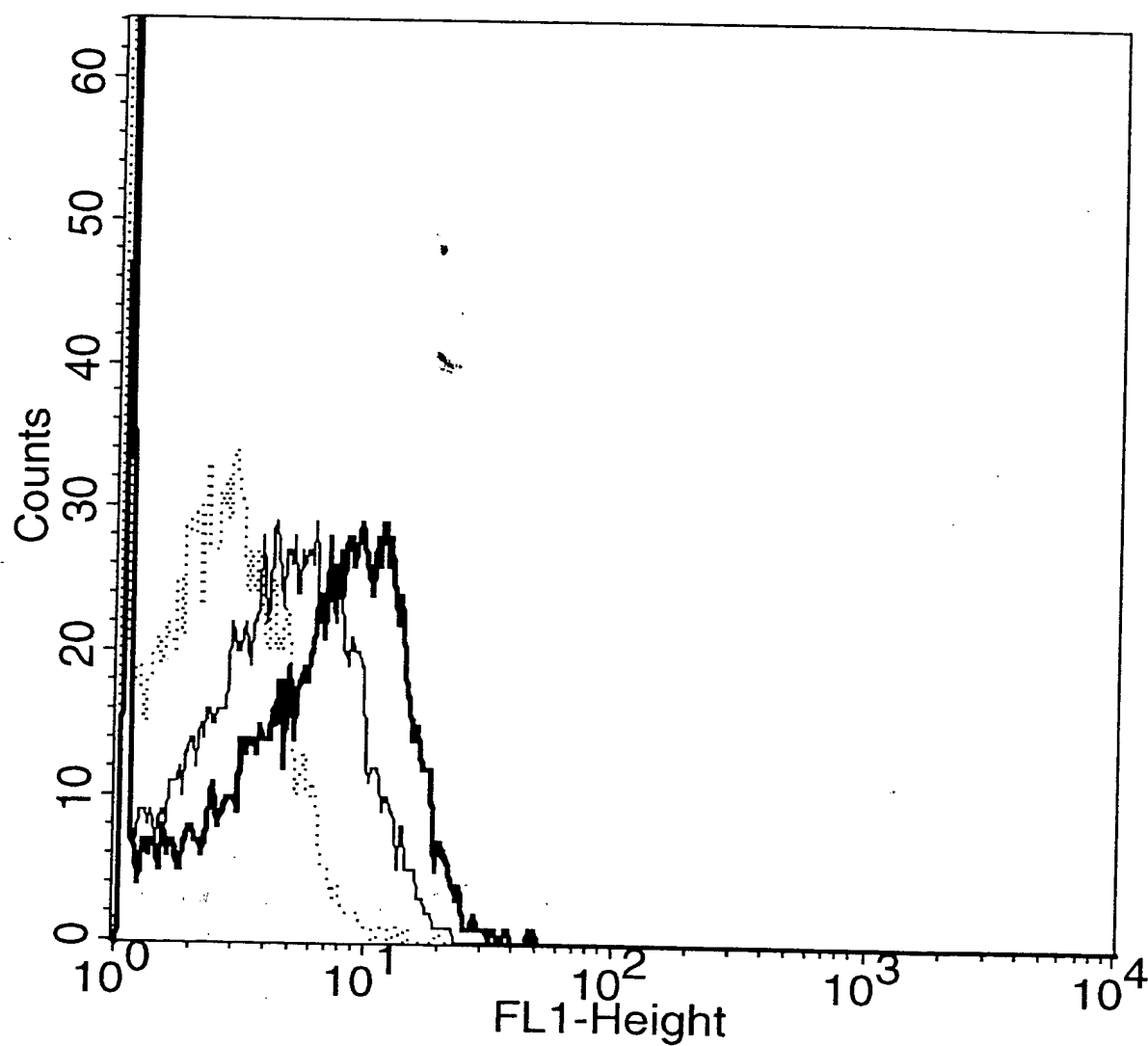


Figure 42



----- neg. control
—— 50µg/ml Heterominibody
—— 400µg/ml Heterominibody

Figure 43

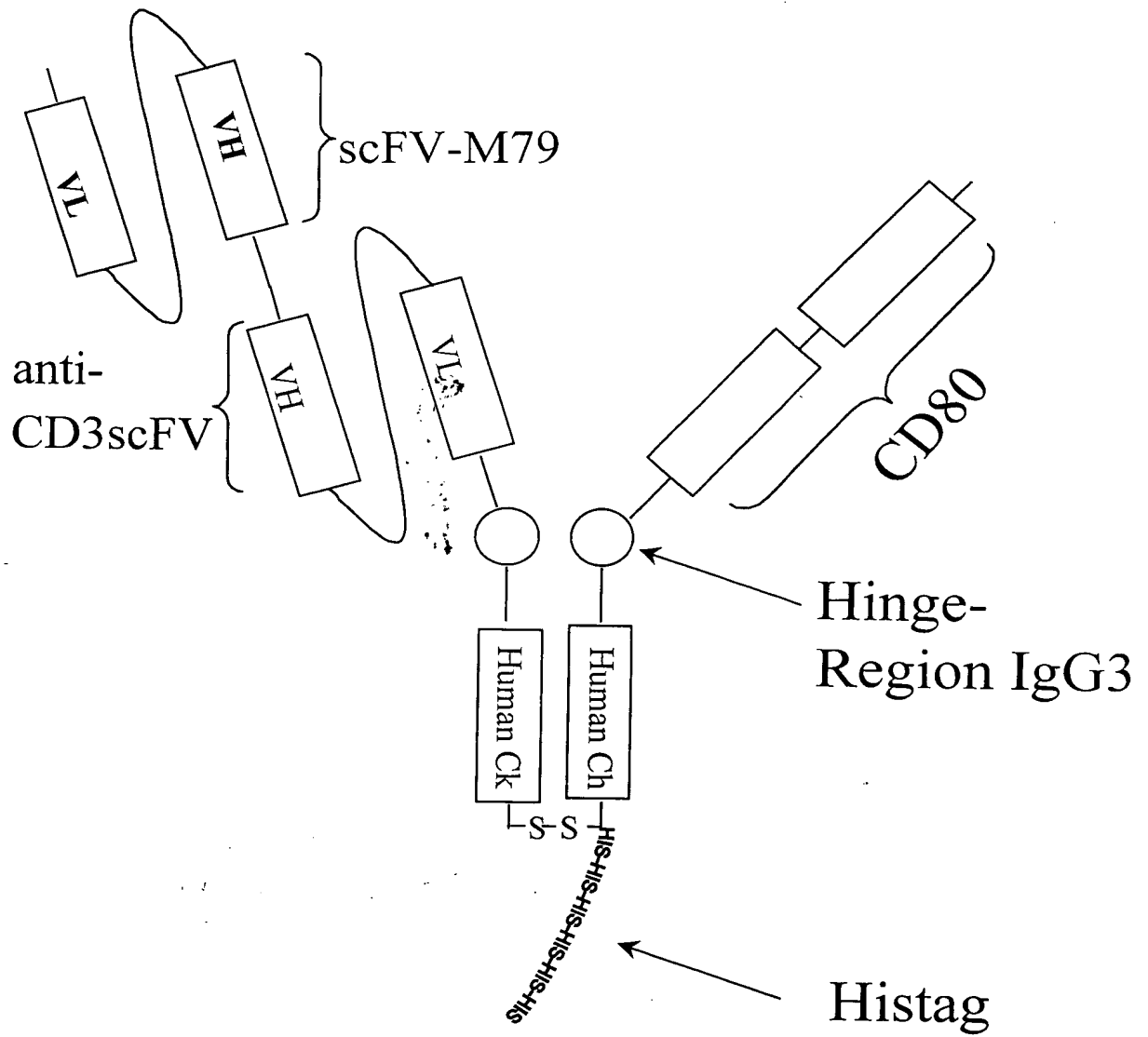
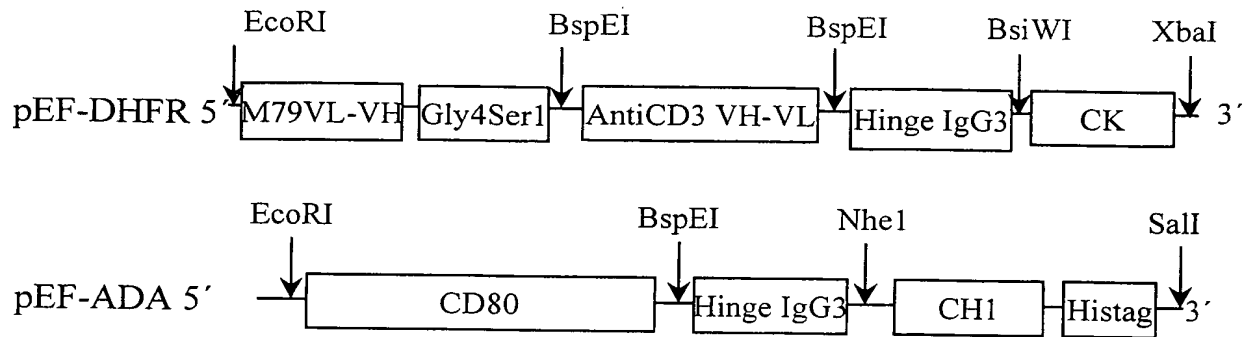


Fig 44



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Figure 45

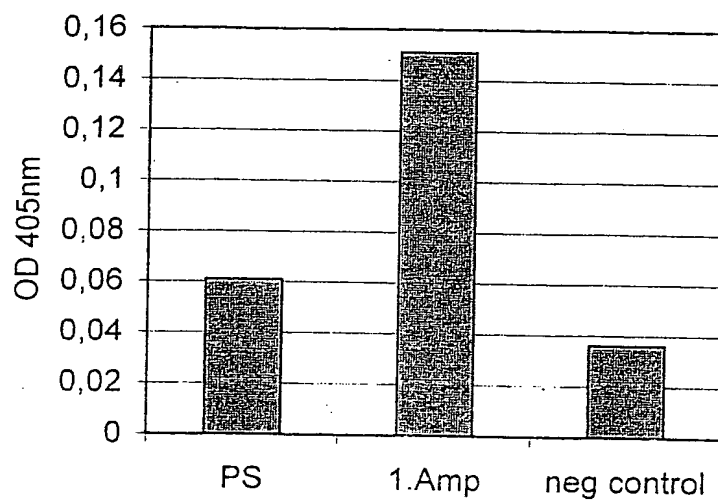
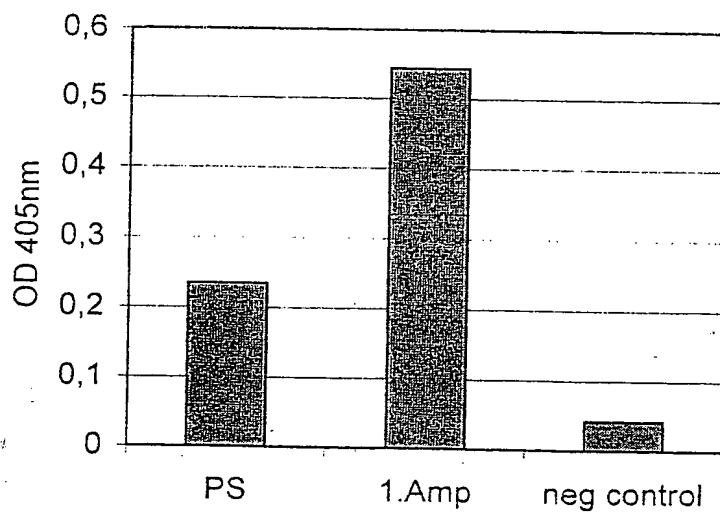


Figure 46



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Figure 47:

5'	EcoRI			9			18			27			36			45			54		
	GAA	TTC	ACC	ATG	GGA	TGG	AGC	TGT	ATC	ATC	CTC	TTC	TTG	GTA	GCA	ACA	GCT	ACA			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
				M	G	W	S	C	I	I	L	F	L	V	A	T	A	T			
	63			72			81			90			99			108					
	GGT	GTA	CAC	TCC	GAT	ATC	CAG	CTG	ACC	CAG	TCT	CAA	AAA	TTC	ATG	TCC	ACA	TCA			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	G	V	H	S	D	I	Q	L	T	Q	S	Q	K	F	M	S	T	S			
	117			126			135			144			153			162					
	GTA	GGA	GAC	AGG	GTC	AGC	GTC	ACC	TGC	AAG	GCC	AGT	CAG	AAT	GTG	GGT	ACT	AAT			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	V	G	D	R	V	S	V	T	C	K	A	S	Q	N	V	G	T	N			
	171			180			189			198			207			216					
	GTA	GCC	TGG	TAT	CAA	CAG	AAA	CCA	GCG	CAA	TCT	CCT	AAA	GCA	CTG	ATT	TAC	TCG			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	V	A	W	Y	Q	Q	K	P	G	Q	S	P	K	A	L	I	Y	S			
	225			234			243			252			261			270					
	GCA	TCC	TAC	CGG	TAC	AGT	GGA	GTC	CCT	GAT	CGC	TTC	ACA	GGC	AGT	GGA	TCT	GCG			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	A	S	Y	R	Y	S	G	V	P	D	R	F	T	G	S	G	S	G			
	279			288			297			306			315			324					
	ACA	GAT	TTC	ACT	CTC	ACC	ATC	AGC	AAT	GTG	CAG	TCT	GAA	GAC	TTG	GCA	CAG	TAT			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	T	D	F	T	L	T	I	S	N	V	Q	S	E	D	L	A	E	Y			
	333			342			351			360			369			378					
	TTC	TGT	CAG	CAA	TAT	AAC	AGC	TAT	CCG	CTC	ACG	TTC	GGT	GCT	GGG	ACC	AAG	CTC			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	F	C	Q	Q	Y	N	S	Y	P	L	T	F	G	A	G	T	K	L			
	387			396			405			414			423			432					
	GAG	ATC	AAA	GGT	GGT	GGT	GGT	TCT	GGC	GGC	GGC	GGC	TCC	GGT	GGT	GGT	GGT	TCT			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	E	I	K	G	G	G	G	S	G	G	G	G	S	G	G	G	G	S			
	441			450			459			468			477			486					
	CAG	GTG	AAA	CTG	CAG	GAG	TCA	GGA	CCT	GGC	CTA	GTG	CAG	CCC	TCA	CAG	AGC	CTG			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	Q	V	K	L	Q	E	S	G	P	G	L	V	Q	P	S	Q	S	L			
	495			504			513			522			531			540					
	TCC	ATC	ACC	TGC	ACA	GTC	TCT	GGT	TTC	TCA	TTA	ACT	AGC	TAT	GGT	GTA	CAC	TGG			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	S	I	T	C	T	V	S	G	F	S	L	T	S	Y	G	V	H	W			
	549			558			567			576			585			594					
	GTT	CGC	CAG	TCT	CCA	GGA	AAG	GGT	CTG	GAG	TGG	CTG	GGA	GTG	ATA	TGG	AGT	GGT			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	V	R	Q	S	P	G	K	G	L	E	W	L	G	V	I	W	S	G			
	603			612			621			630			639			648					
	GGA	AGC	ACA	GAC	TAT	AAT	GCA	GCT	TTC	ATA	TCC	AGA	CTG	AGC	ATC	AGC	AAG	GAC			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	G	S	T	D	Y	N	A	A	F	I	S	R	L	S	I	S	K	D			

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Figure 47 cont.

		657		666		675		684		693		702					
AAT	TCC	AAG	AGC	CAA	GTT	TTC	TTT	AAA	ATG	AAC	AGT	CTG	CAA	GCT	AAT	GAC	ACA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
N	S	K	S	Q	V	F	F	K	M	N	S	L	Q	A	N	D	T
		711		720		729		738		747		756					
GCC	ATA	TAT	TAC	TGT	GCC	AGA	ATG	GAG	AAC	TGG	TCG	TTT	GCT	TAC	TGG	GGC	CAA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
A	I	Y	Y	C	A	R	M	E	N	W	S	F	A	Y	W	G	Q
		765		774		783		792		801		810					
GGG	ACC	ACG	GTC	ACC	GTC	TCC	GAA	TTC	CCC	AAA	CCT	AGC	ACC	CCC	CCT	GGC	AGC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
G	T	T	V	T	V	S	E	F	P	K	P	S	T	P	P	G	S
		819		828		837		846		855		864					
AGT	GGT	GAA	CTG	GAA	GAG	CTG	CTT	AAG	CAT	CTT	AAA	GAA	CTT	CTG	AAG	GGC	CCC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
S	G	E	L	E	E	L	L	K	H	L	K	E	L	L	K	G	P
		873		882		891		900		909		918					
CGC	AAA	GGC	GAA	CTC	GAG	GAA	CTG	CTG	AAA	CAT	CTG	AAG	GAG	CTG	CTT	AAA	GGT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
R	K	G	E	L	E	E	L	L	K	H	L	K	E	L	L	K	G
		927		936		945		954		963		972					
GGG	AGC	GGA	GGC	GCG	CCG	GCA	CCT	ACT	TCA	AGT	TCT	ACA	AAG	AAA	ACA	CAG	CTA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
G	S	G	G	A	P	A	P	T	S	S	S	T	K	K	T	Q	L
		981		990		999		1008		1017		1026					
CAA	CTG	GAG	CAT	TTA	CTG	CTG	GAT	TTA	CAG	ATG	ATT	TTG	AAT	GGA	ATT	AAT	AAT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Q	L	E	H	L	L	L	D	L	Q	M	I	L	N	G	I	N	N
		1035		1044		1053		1062		1071		1080					
TAC	AAG	AAT	CCC	AAA	CTC	ACC	AGG	ATG	CTC	ACA	TTT	AAG	TTT	TAC	ATG	CCC	AAG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Y	K	N	P	K	L	T	R	M	L	T	F	K	F	Y	M	P	K
		1089		1098		1107		1116		1125		1134					
AAG	GCC	ACA	GAA	CTG	AAA	CAT	CTT	CAG	TGT	CTA	GAA	GAA	GAA	CTC	AAA	CCT	CTG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
K	A	T	E	L	K	H	L	Q	C	L	E	E	E	L	K	P	L
		1143		1152		1161		1170		1179		1188					
GAG	GAA	GTG	CTA	AAT	TTA	GCT	CAA	AGC	AAA	AAC	TTT	CAC	TTA	AGA	CCC	AGG	GAC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
E	E	V	L	N	L	A	Q	S	K	N	F	H	L	R	P	R	D
		1197		1206		1215		1224		1233		1242					
TTA	ATC	AGC	AAT	ATC	AAC	GTA	ATA	GTT	CTG	GAA	CTA	AAG	GGA	TCT	GAA	ACA	ACA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
L	I	S	N	I	N	V	I	V	L	E	L	K	G	S	E	T	T
		1251		1260		1269		1278		1287		1296					
TTC	ATG	TGT	GAA	TAT	GCT	GAT	GAG	ACA	GCA	ACC	ATT	GTA	GAA	TTT	CTG	AAC	AGA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
F	M	C	E	Y	A	D	E	T	A	T	I	V	E	F	L	N	R

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Figure 47 cont.

1305			1314			1323			1332			1341			1350		
TGG	ATT	ACC	TTT	TGT	CAA	AGC	ATC	ATC	TCA	ACA	CTG	ACT	GAC	GTC	CAT	CAC	CAT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
W	I	T	F	C	Q	S	I	I	S	T	L	T	D	V	H	H	H
				SalI													
1359																	
CAC	CAT	CAC	TGA	TAA	GTC	GAC											
---	---	---	---	---	---	---											
H	H	H	*	*													

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Figure 48:

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EcoRI																			
5'	GAA	TTC	ACC	ATG	GGA	TGG	AGC	TGT	ATC	ATC	CTC	TTC	TTG	GTA	GCA	ACA	GCT	ACA	
				M	G	W	S	C	I	I	L	F	L	V	A	T	A	T	
	GGT	GTA	CAC	TCC	GAT	ATC	CAG	CTG	ACC	CAG	TCT	CAA	AAA	TTC	ATG	TCC	ACA	TCA	
	G	V	H	S	D	I	Q	L	T	Q	S	Q	K	F	M	S	T	S	
	GTA	GGA	GAC	AGG	GTC	AGC	GTC	ACC	TGC	AAG	GCC	AGT	CAG	AAT	GTG	GGT	ACT	AAT	
	V	G	D	R	V	S	V	T	C	K	A	S	Q	N	V	G	T	N	
	GTA	GCC	TGG	TAT	CAA	CAG	AAA	CCA	GGG	CAA	TCT	CCT	AAA	GCA	CTG	ATT	TAC	TCG	
	V	A	W	Y	Q	Q	K	P	G	Q	S	P	K	A	L	I	Y	S	
	GCA	TCC	TAC	CGG	TAC	AGT	GGA	GTC	CCT	GAT	CGC	TTC	ACA	GGC	AGT	GGA	TCT	GGG	
	A	S	Y	R	Y	S	G	V	P	D	R	F	T	G	S	G	S	G	
	ACA	GAT	TTC	ACT	CTC	ACC	ATC	AGC	AAT	GTG	CAG	TCT	GAA	GAC	TTG	GCA	GAG	TAT	
	T	D	F	T	L	T	I	S	N	V	Q	S	E	D	L	A	E	Y	
	TTC	TGT	CAG	CAA	TAT	AAC	AGC	TAT	CCG	CTC	ACG	TTC	GGT	GCT	GGG	ACC	AAG	CTC	
	F	C	Q	Q	Y	N	S	Y	P	L	T	F	G	A	G	T	K	L	
	GAG	ATC	AAA	GGT	GGT	GGT	GGT	TCT	GGC	GGC	GGC	GGC	TCC	GGT	GGT	GGT	GGT	TCT	
	E	I	K	G	G	G	G	S	G	G	G	G	S	G	G	G	G	S	
	CAG	GTG	AAA	CTG	CAG	GAG	TCA	GGA	CCT	GGC	CTA	GTG	CAG	CCC	TCA	CAG	AGC	CTG	
	Q	V	K	L	Q	E	S	G	P	G	L	V	Q	P	S	Q	S	L	
	TCC	ATC	ACC	TGC	ACA	GTC	TCT	GGT	TTC	TCA	TTA	ACT	AGC	TAT	GGT	GTA	CAC	TGG	
	S	I	T	C	T	V	S	G	F	S	L	T	S	Y	G	V	H	W	
	GTT	CGC	CAG	TCT	CCA	GGA	AAG	GGT	CTG	GAG	TGG	CTG	GGA	GTG	ATA	TGG	AGT	GGT	
	V	R	Q	S	P	G	K	G	L	E	W	L	G	V	I	W	S	G	
	GGA	AGC	ACA	GAC	TAT	AAT	GCA	GCT	TTC	ATA	TCC	AGA	CTG	AGC	ATC	AGC	AAG	GAC	
	G	S	T	D	Y	N	A	A	F	I	S	R	L	S	I	S	K	D	

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Figure 48 cont.

AAT	TCC	657	AAG	AGC	CAA	666	GTT	TTC	TTT	675	AAA	ATG	AAC	684	AGT	CTG	CAA	693	GCT	AAT	GAC	702	ACA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
N	S	K	S	Q	V	F	F	K	M	N	S	L	Q	A	N	D	T						
GCC	ATA	711	TAT	TAC	TGT	720	GCC	AGA	ATG	729	GAG	AAC	TGG	738	TCG	TTT	GCT	747	TAC	TGG	GGC	756	CAA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
A	I	Y	Y	C	A	R	M	E	N	W	S	F	A	Y	W	G	Q						
GGG	ACC	765	ACG	GTC	ACC	774	GTC	TCC	GAA	783	TTC	ACC	CCG	792	CTG	GGT	GAC	801	ACC	ACC	CAC	810	ACC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
G	T	T	V	T	V	S	E	F	T	P	L	G	D	T	T	H	T						
TCC	GGA	819	AAA	CCA	CTG	828	GAT	GGA	GAA	837	TAT	TTC	ACC	846	CTT	CAG	ATC	855	CGT	GGG	CGT	864	GAG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
S	G	K	P	L	D	G	E	Y	F	T	L	Q	I	R	G	R	E						
CGC	TTC	873	GAG	ATG	TTC	882	CGA	GAG	CTG	891	AAT	GAG	GCC	900	TTG	GAA	CTC	909	AAG	GAT	GCC	918	CAG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
R	F	E	M	F	R	E	L	N	E	A	L	E	L	K	D	A	Q						
GCT	GGG	927	AAG	GAG	CCA	936	GGG	AGC	GGA	945	GGC	GCG	CCG	954	GCA	CCT	ACT	963	TCA	AGT	TCT	972	TCT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
A	G	K	E	P	G	G	S	G	G	A	P	A	P	T	S	S	S						
ACA	AAG	981	AAA	ACA	CAG	990	CTA	CAA	CTG	999	GAG	CAT	TTA	1008	CTG	CTG	GAT	1017	TTA	CAG	ATG	1026	ATT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
T	K	K	T	Q	L	Q	L	E	H	L	L	L	D	L	Q	M	I						
TTG	AAT	1035	GGA	ATT	AAT	1044	AAT	TAC	AAG	1053	AAT	CCC	AAA	1062	CTC	ACC	AGG	1071	ATG	CTC	ACA	1080	TTT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
L	N	G	I	N	N	Y	K	N	P	K	L	T	R	M	L	T	F						
AAG	TTT	1089	TAC	ATG	CCC	1098	AAG	AAG	GCC	1107	ACA	GAA	CTG	1116	AAA	CAT	CTT	1125	CAG	TGT	CTA	1134	GAA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
K	F	Y	M	P	K	K	A	T	E	L	K	H	L	Q	C	L	E						
GAA	GAA	1143	CTC	AAA	CCT	1152	CTG	GAG	GAA	1161	GTG	CTA	AAT	1170	TTA	GCT	CAA	1179	AGC	AAA	AAC	1188	TTT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
E	E	L	K	P	L	E	E	V	L	N	L	A	Q	S	K	N	F						
CAC	TTA	1197	AGA	CCC	AGG	1206	GAC	TTA	ATC	1215	AGC	AAT	ATC	1224	AAC	GTA	ATA	1233	GTT	CTG	GAA	1242	CTA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
H	L	R	P	R	D	L	I	S	N	I	N	V	I	V	L	E	L						
AAG	GGA	1251	TCT	GAA	ACA	1260	ACA	TTC	ATG	1269	TGT	GAA	TAT	1278	GCT	GAT	GAG	1287	ACA	GCA	ACC	1296	ATT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
K	G	S	E	T	T	F	M	C	E	Y	A	D	E	T	A	T	I						

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Figure 48 cont.

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		1305			1314			1323			1332			1341			1350
GTA	GAA	TTT	CTG	AAC	AGA	TGG	ATT	ACC	TTT	TGT	CAA	AGC	ATC	ATC	TCA	ACA	CTG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
V	E	F	L	N	R	W	I	T	F	C	Q	S	I	I	S	T	L
		1359			1368			1377			Sall						
ACT	GAC	GTC	CAT	CAC	CAT	CAC	CAT	CAC	TGA	TAA	GTC	GAC					
---	---	---	---	---	---	---	---	---	---	---	---	---					
T	D	V	H	H	H	H	H	H	*	*							

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Figure 49:

5'	EcoRI		9		18		27		36		45		54					
	GAA	TTC	ACC	ATG	GGA	TGG	AGC	TGT	ATC	ATC	CTC	TTC	TTG	GTA	GCA	ACA	GCT	ACA
				M	G	W	S	C	I	I	L	F	L	V	A	T	A	T
	63		72		81		90		99		108							
	GGT	GTA	CAC	TCC	GAT	ATC	CAG	CTG	ACC	CAG	TCT	CCA	GCA	ATC	ATG	TCT	GCA	TCT
	G	V	H	S	D	I	Q	L	T	Q	S	P	A	I	M	S	A	S
	117		126		135		144		153		162							
	CCA	GGG	GAA	AAG	GTC	ACC	ATG	ACC	TGC	AGG	GCC	AGC	TCA	AGT	GTT	AGT	TCC	AGT
	P	G	E	K	V	T	M	T	C	R	A	S	S	S	V	S	S	S
	171		180		189		198		207		216							
	TAC	TTG	CAC	TGG	TAC	CAG	CAG	AAG	TCA	GGT	GCC	TCC	CCC	AAA	CTC	TGG	ATT	TAT
	Y	L	H	W	Y	Q	Q	K	S	G	A	S	P	K	L	W	I	Y
	225		234		243		252		261		270							
	AGC	ACA	TCC	AAC	TTG	GCT	TCT	GGA	GTC	CCT	GCT	CGC	TTC	AGT	GGC	AGT	GGG	TCT
	S	T	S	N	L	A	S	G	V	P	A	R	F	S	G	S	G	S
	279		288		297		306		315		324							
	GGG	ACC	TCT	TAC	TCT	CTC	ACA	ATC	AGC	AGT	GTG	GAG	GCT	GAA	GAT	GCT	GCC	ACT
	G	T	S	Y	S	L	T	I	S	S	V	E	A	E	D	A	A	T
	333		342		351		360		369		378							
	TAT	TAC	TGC	CAG	CAG	TAC	AGT	GGT	TAC	CCG	TAC	ACG	TTC	GGA	GGG	GGG	ACC	AAG
	Y	Y	C	Q	Q	Y	S	G	Y	P	Y	T	F	G	G	G	T	K
	387		396		405		414		423		432							
	CTC	GAG	ATC	AAA	GGT	GGT	GGT	GGT	TCT	GGC	GGC	GGC	GGC	TCC	GGT	GGT	GGT	GGT
	L	E	I	K	G	G	G	G	S	G	G	G	G	S	G	G	G	G
	441		450		459		468		477		486							
	TCT	CAG	GTG	AAA	CTG	CAG	GAG	TCT	GGG	GCT	GAG	CTT	GTG	AAG	CCT	GGG	GCT	TCA
	S	Q	V	K	L	Q	E	S	G	A	E	L	V	K	P	G	A	S
	495		504		513		522		531		540							
	GTG	AAG	CTG	TCC	TGC	AAG	GCT	TCT	GGC	TAC	ACC	CTC	ACC	AGC	TAC	TGG	TTG	CAC
	V	K	L	S	C	K	A	S	G	Y	T	L	T	S	Y	W	L	H
	549		558		567		576		585		594							
	TGG	GTG	AAG	CAG	TGG	CCT	GGA	CGA	GGC	CTT	GAG	TGG	ATT	GGA	AGG	ATT	GAT	CCC
	W	V	K	Q	W	P	G	R	G	L	E	W	I	G	R	I	D	P
	603		612		621		630		639		648							
	AAT	AGT	GGT	GGT	ACT	AAG	TAC	GAT	GAG	AAG	TTC	AAG	AGC	AAG	GCC	ACA	CTG	ACT
	N	S	G	G	T	K	Y	D	E	K	F	K	S	K	A	T	L	T

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Figure 49 cont.

657	666	675	684	693	702
GTA GAC AAA CCC TCC	AGC ACA GCC TAC	ATG CAG CTC AGC AGC	CTG ACA TCT	GAG	
V D K P S	S T A Y M Q	L S S L T S	E		
711	720	729	738	747	756
GAC TCT GCG GTC TAT	TAT TGT GCA AGA	TGG GAC TAC TGG GGC	CAA GGG ACC	ACG	
D S A V Y	Y C A R W D	Y W G Q G T	T		
765	774	783	792	801	810
GTC ACC GTC TCC TCC	GGA ACC CCG CTG	GGT GAC ACC ACC	CAC ACT AGT GGA	AAA	
V T V S S	G T P L G D	T T H T S G	K		
819	828	837	846	855	864
CCA CTG GAT GGA GAA	TAT TTC ACC CTT	CAG ATC CGT GGG	CGT GAG CGC TTC	GAG	
P L D G E	Y F T L Q I	R G R E R F	E		
873	882	891	900	909	918
ATG TTC CGA GAG CTG	AAT GAG GCC TTG	GAA CTC AAG GAT	GCC CAG GCT GGG	AAG	
M F R E L	N E A L E L	K D A Q A G	K		
927	936	945	954	963	972
GAG CCA GGG GGG TCC	GGA GGT GGT GGT	AGC ACC CAA GTG	TGC ACC GGC ACA	GAC	
E P G G S	G G G G S T	Q V C T G T	D		
981	990	999	1008	1017	1026
ATG AAG CTG CGG CTC	CCT GCC AGT CCC	GAG ACC CAC CTG	GAC ATG CTC CGC	CAC	
M K L R L	P A S P E T	H L D M L R	H		
1035	1044	1053	1062	1071	1080
CTC TAC CAG GGC TGC	CAG GTG GTG CAG	GGA AAC CTG GAA	CTC ACC TAC CTG	CCC	
L Y Q G C	Q V V Q G N	L E L T Y L	P		
1089	1098	1107	1116	1125	1134
ACC AAT GCC AGC CTG	TCC TTC CTG CAG	GAT ATC CAG GAG	GTG CAG GGC TAC	GTG	
T N A S L	S F L Q D I	Q E V Q G Y	V		
1143	1152	1161	1170	1179	1188
CTC ATC GCT CAC AAC	CAA GTG AGG CAG	GTC CCA CTG CAG	AGG CTG CGG ATT	GTG	
L I A H N	Q V R Q V P	L Q R L R I	V		
1197	1206	1215	1224	1233	1242
CGA GGC ACC CAG CTC	TTT GAG GAC AAC	TAT GCC CTG GCC	GTG CTA GAC AAT	GGA	
R G T Q L	F E D N Y A	L A V L D N	G		
1251	1260	1269	1278	1287	1296
GAC CCG CTG AAC AAT	ACC ACC CCT GTC	ACA GGG GCC TCC	CCA GGA GCC CTG	CGG	
D P L N N	T T P V T G	A S P G G L	R		

Figure 49 cont.

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1305	1314	1323	1332	1341	1350
GAG CTG CAG CTT CGA AGC CTC ACA GAG ATC TTG AAA GGA GGG GTC TTG ATC CAG					
E L Q L R S L T E I L K G G V L I Q					
1359	1368	1377	1386	1395	1404
CGG AAC CCC CAG CTC TGC TAC CAG GAC ACG ATT TTG TGG AAG GAC ATC TTC CAC					
R N P Q L C Y Q D T I L W K D I F H					
1413	1422	1431	1440	1449	1458
AAG AAC AAC CAG CTG GCT CTC ACA CTG ATA GAC ACC AAC CGC TCT CGG GCC TGC					
K N N Q L A L T L I D T N R S R A C					
1467	1476	1485	1494	1503	1512
CAC CCC TGT TCT CCG ATG TGT AAG GGC TCC CGC TGC TGG GGA GAG AGT TCT GAG					
H P C S P M C K G S R C W G E S S E					
1521	1530	1539	1548	1557	1566
GAT TGT CAG AGC CTG ACG CGC ACT GTC TGT GCC GGT GGC TGT GCC CGC TGC AAG					
D C Q S L T R T V C A G G C A R C K					
1575	1584	1593	1602	1611	1620
GGG CCA CTG CCC ACT GAC TGC TGC CAT GAG CAG TGT GCT GCC GGC TGC ACG GGC					
G P L P T D C C H E Q C A A G C T G					
1629	1638	1647	1656	1665	1674
CCC AAG CAC TCT GAC TGC CTG GCC TGC CTC CAC TTC AAC CAC AGT GGC ATC TGT					
P K H S D C L A C L H F N H S G I C					
1683	1692	1701	1710	1719	1728
GAG CTG CAC TGC CCA GCC CTG GTC ACC TAC AAC ACA GAC ACG TTT GAG TCC ATG					
E L H C P A L V T Y N T D T F E S M					
1737	1746	1755	1764	1773	1782
CCC AAT CCC GAG GGC CGG TAT ACA TTC GGC GCC AGC TGT GTG ACT GCC TGT CCC					
P N P E G R Y T F G A S C V T A C P					
1791	1800	1809	1818	1827	1836
TAC AAC TAC CTT TCT ACG GAC GTG GGA TCC TGC ACC CTC GTC TGC CCC CTG CAC					
Y N Y L S T D V G S C T L V C P L H					
1845	1854	1863	1872	1881	1890
AAC CAA GAG GTG ACA GCA GAG GAT GGA ACA CAG CGG TGT GAG AAG TGC AGC AAG					
N Q E V T A E D G T Q R C E K C S K					
1899	1908	1917	1926	1935	1944
CCC TGT GCC CGA GTG TGC TAT GGT CTG GGC ATG GAG CAC TTG CGA GAG GTG AGG					
P C A R V C Y G L G M E H L R E V R					

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Figure 49 cont.

1953				1962			1971			1980			1989			1998		
GCA	GTT	ACC	AGT	GCC	AAT	ATC	CAG	GAG	TTT	GCT	GGC	TGC	AAG	AAG	ATC	TTT	GGG	
A	V	T	S	A	N	I	Q	E	F	A	G	C	K	K	I	F	G	
2007				2016			2025			2034			2043			2052		
AGC	CTG	GCA	TTT	CTG	CCG	GAG	AGC	TTT	GAT	GGG	GAC	CCA	GCC	TCC	AAC	ACT	GCC	
S	L	A	F	L	P	E	S	F	D	G	D	P	A	S	N	T	A	
2061				2070			2079			2088			2097			2106		
CCG	CTC	CAG	CCA	GAG	CAG	CTC	CAA	GTG	TTT	GAG	ACT	CTG	GAA	GAG	ATC	ACA	GGT	
P	L	Q	P	E	Q	L	Q	V	F	E	T	L	E	E	I	T	G	
2115				2124			2133			2142			2151			2160		
TAC	CTA	TAC	ATC	TCA	GCA	TGG	CCG	GAC	AGC	CTG	CCT	GAC	CTC	AGC	GTC	TTC	CAG	
Y	L	Y	I	S	A	W	P	D	S	L	P	D	L	S	V	F	Q	
2169				2178			2187			2196			2205			2214		
AAC	CTG	CAA	GTA	ATC	CGG	GGA	CGA	ATT	CTG	CAC	AAT	GGC	GCC	TAC	TCG	CTG	ACC	
N	L	Q	V	I	R	G	R	I	L	H	N	G	A	Y	S	L	T	
2223				2232			2241			2250			2259			2268		
CTG	CAA	GGG	CTG	GGC	ATC	AGC	TGG	CTG	GGG	CTG	CGC	TCA	CTG	AGG	GAA	CTG	GGC	
L	Q	G	L	G	I	S	W	L	G	L	R	S	L	R	E	L	G	
2277				2286			2295			2304			2313			2322		
AGT	GGA	CTG	GCC	CTC	ATC	CAC	CAT	AAC	ACC	CAC	CTC	TGC	TTC	GTG	CAC	ACG	GTG	
S	G	L	A	L	I	H	H	N	T	H	L	C	F	V	H	T	V	
2331				2340			2349			2358			2367			2376		
CCC	TGG	GAC	CAG	CTC	TTT	CGG	AAC	CCG	CAC	CAA	GCT	CTG	CTC	CAC	ACT	GCC	AAC	
P	W	D	Q	L	F	R	N	P	H	Q	A	L	L	H	T	A	N	
2385				2394			2403			2412			2421			2430		
CGG	CCA	GAG	GAC	GAG	TGT	GTG	GGC	GAG	GGC	CTG	GCC	TGC	CAC	CAG	CTG	TGC	GCC	
R	P	E	D	E	C	V	G	E	G	L	A	C	H	Q	L	C	A	
2439				2448			2457			2466			2475			2484		
CGA	GGG	CAC	TGC	TGG	GCT	CCA	GGG	CCC	ACC	CAG	TGT	GTC	AAC	TGC	AGC	CAG	TTC	
R	G	H	C	W	G	P	G	P	T	Q	C	V	N	C	S	Q	F	
2493				2502			2511			2520			2529			2538		
CTT	CGG	GGC	CAG	GAG	TGC	GTG	GAG	GAA	TGC	CGA	GTA	CTG	CAG	GGG	CTC	CCC	AGG	
L	R	G	Q	E	C	V	E	E	C	R	V	L	Q	G	L	P	R	
2547				2556			2565			2574			2583			2592		
GAG	TAT	GTG	AAT	GCC	AGG	CAC	TGT	TTG	CCG	TGC	CAC	CCT	GAG	TGT	CAG	CCC	CAG	
E	Y	V	N	A	R	H	C	L	P	C	H	P	E	C	Q	P	Q	

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Figure 49 cont.

2601			2610			2619			2628			2637			2646		
AAT	GGC	TCA	GTG	ACC	TGT	TTT	GGA	CCG	GAG	GCT	GAC	CAG	TGT	GTG	GCC	TGT	GCC
N	G	S	V	T	C	F	G	P	E	A	D	Q	C	V	A	C	A
2655			2664			2673			2682			2691			2700		
CAC	TAT	AAG	GAC	CCT	CCC	TTC	TGC	GTG	GCC	CGC	TGC	CCC	AGC	GGT	GTG	AAA	CCT
H	Y	K	D	P	P	F	C	V	A	R	C	P	S	G	V	K	P
2709			2718			2727			2736			2745			2754		
GAC	CTC	TCC	TAC	ATG	CCC	ATC	TGG	AAG	TTT	CCA	GAT	GAG	GAG	GGC	GCA	TGC	CAG
D	L	S	Y	M	P	I	W	K	F	P	D	E	E	G	A	C	Q
2763			2772			2781			2790			2799			2808		
CCT	TGC	CCC	ATC	AAC	TGC	ACC	CAC	TCC	TGT	GTG	GAC	CTG	GAT	GAC	AAG	GGC	TGC
P	C	P	I	N	C	T	H	S	C	V	D	L	D	D	K	G	C
2817			2826			2835			2844			2853			2862		
CCC	GCC	GAG	CAG	AGA	GCC	AGC	CCT	CTG	ACG	TCC	GGG	CAT	CAT	CAC	CAT	CAT	CAT
P	A	E	Q	R	A	S	P	L	T	S	G	H	H	H	H	H	H
SalI																	
TGA	GTC	GAC	3'														
*																	

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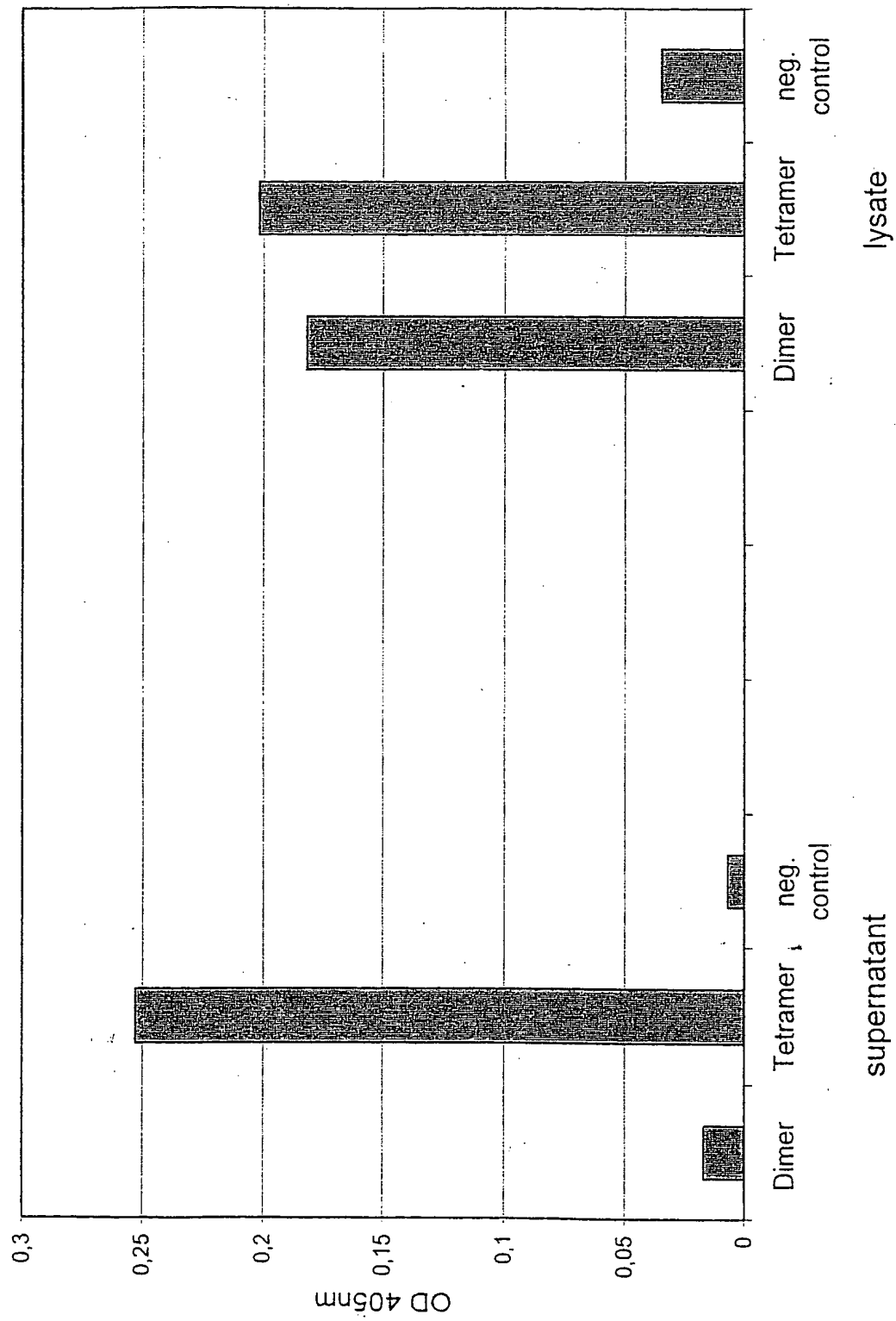
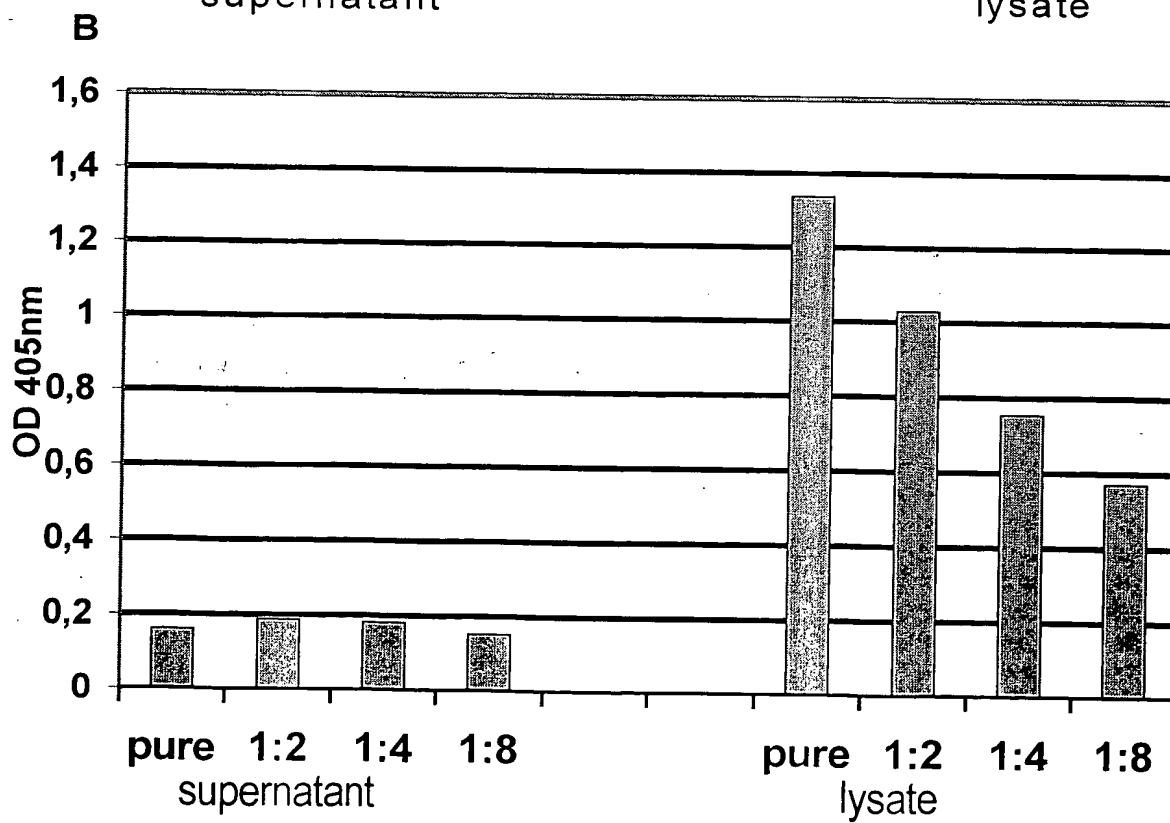
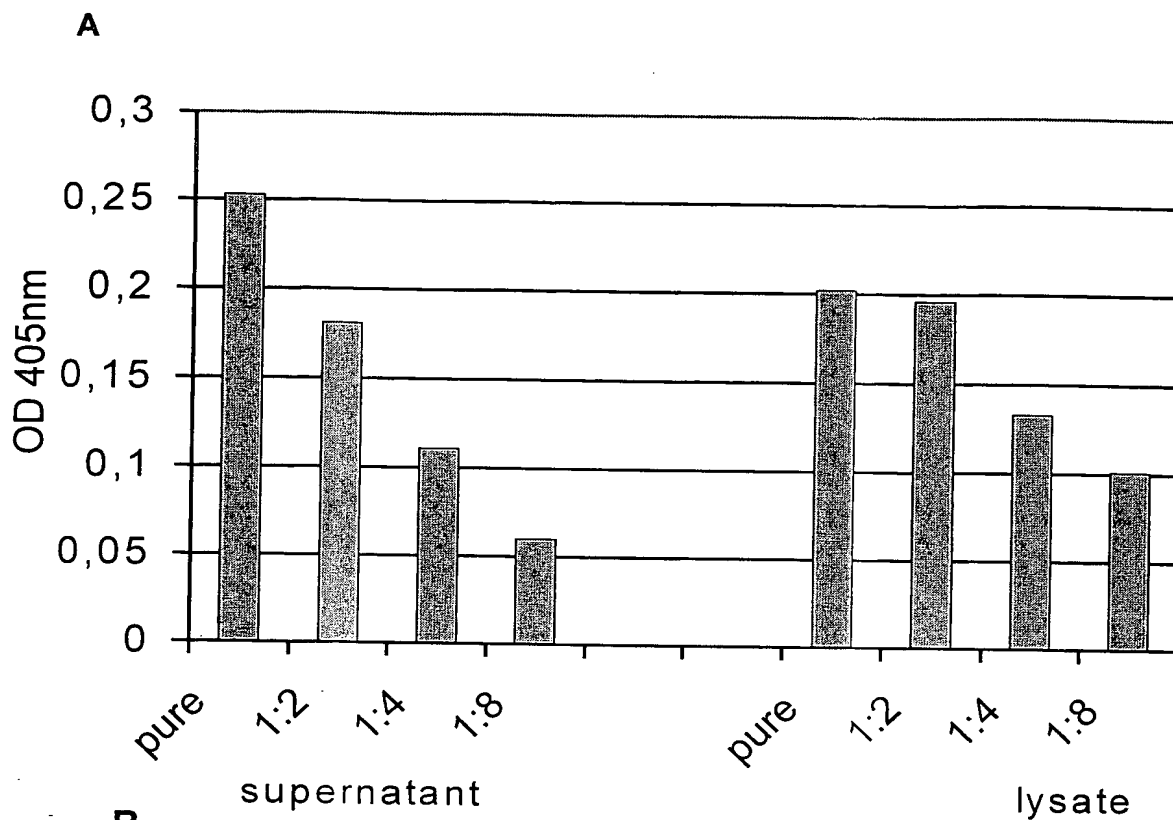


Figure 50

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Figure 51

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N-Terminally Linked Effector Functions



Figure 53

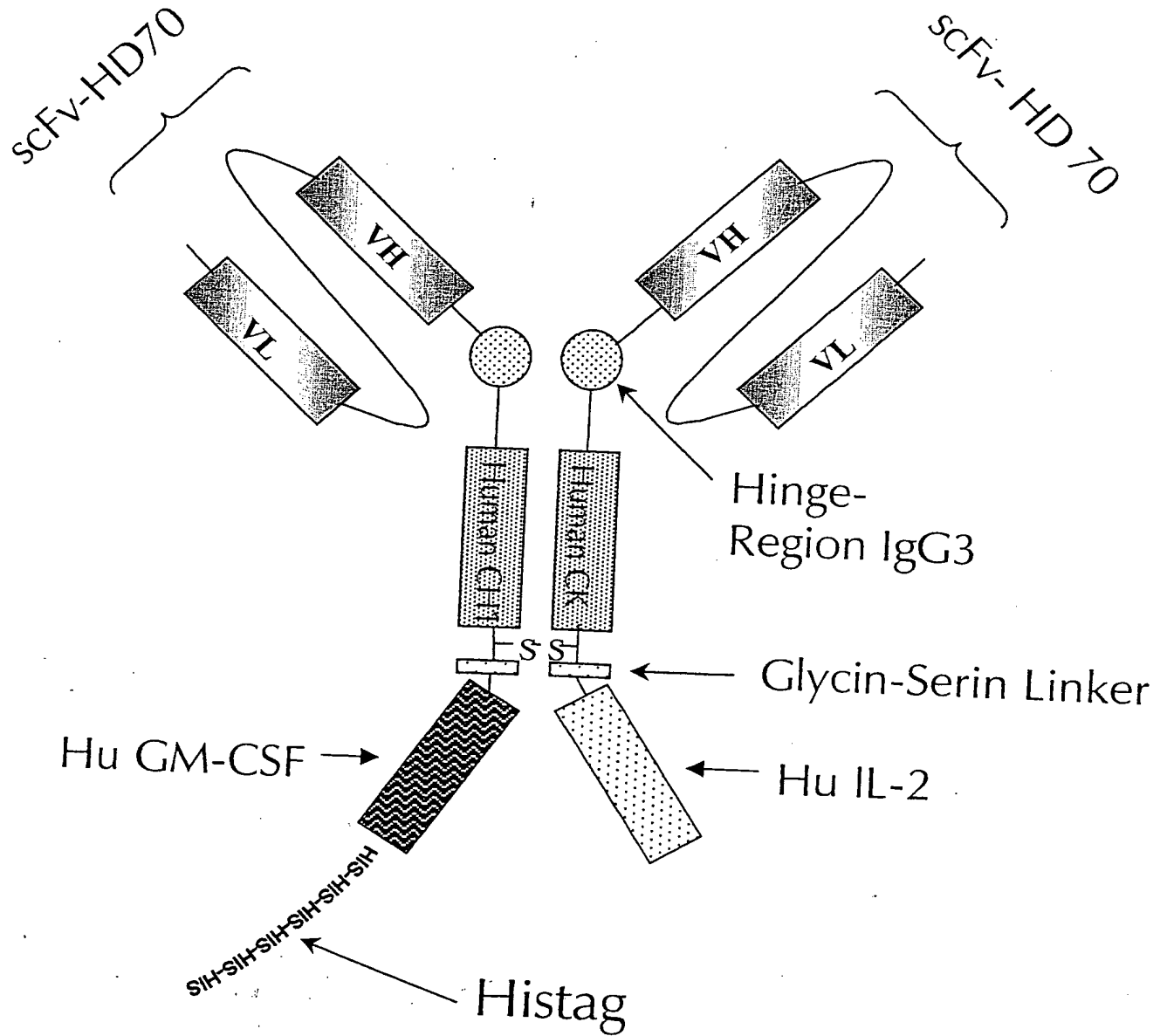
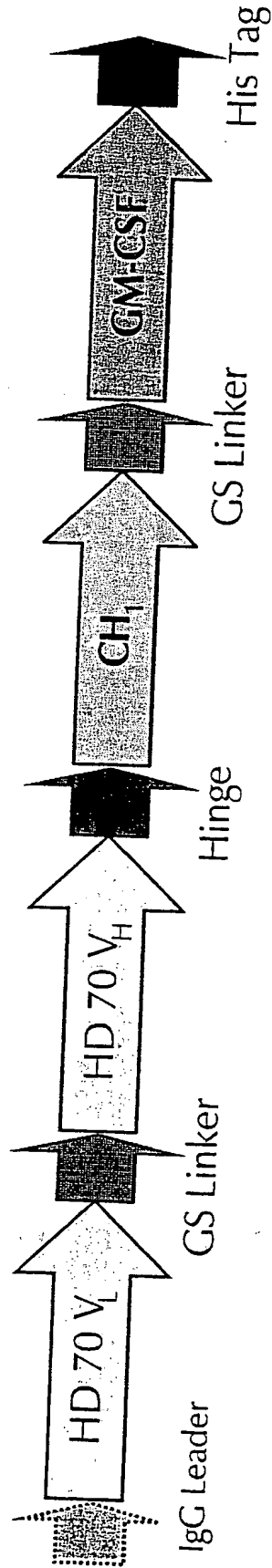


Figure 54

HD 70 scFv - CH1-GM-CSF:



HD 70 scFv - Cκ-IL 2:

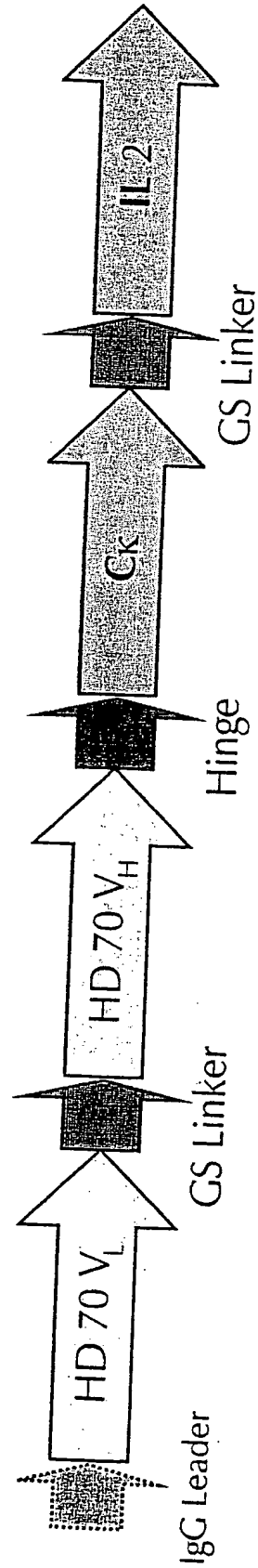


Figure 55a

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```

+3      M   G   W   S   C   I   I
      EcoRI  NcoI
1  TTTTTTCTT CCATTTCAGG TGTCGTGAGG AATTCACCAT GGGATGGAGC TGTATCATCC
   AAAAAAGAA GGTAAGTCC ACAGCACTCC TTAAGTGGTA CCCTACCTCG ACATAGTAGG

+3 L F L V A T A T G V H S E L Q M T Q S P
      BsrGI   SacI
61 TCTTCTTGGT AGCAACAGCT ACAGGTGTAC ACTCCGAGCT CCAGATGACC CAGTCTCCAT
   AGAAGAACCA TCGTTGTGCA TGTCCACATG TGAGGCTCGA GGTCTACTGG GTCAGAGGTA

+3 S S L S A S V G D R V T I T C R A S Q S
121 CCTCCCTGTC TGCATCTGTA GGAGACAGAG TCACCATCAC TTGCCGGGCA AGTCAGAGCA
   GGAGGGACAG ACGTAGACAT CCTCTGTCTC AGTGGTAGTG AACGGCCCGT TCAGTCTCGT

+3 I S S Y L N W Y Q Q K P G Q P P K L L I
      SwaI
181 TTAGCAGCTA TTAAATTGG TATCAGCAGA AACCAGGACA GCCTCCTAAG CTGCTCATTT
   AATCGTCGAT AAATTTAACC ATAGTCGTCT TTGGTCCTGT CGGAGGATTC GACGAGTAA

+3 Y W A S T R E S G V P D R F S G S E S G
      SmaI
241 ACTGGGCATC TACCCGGGAA TCCGGGGTCC CTGACCGATT CAGCGGCAGT GAATCTGGGA
   TGACCCGTAG ATGGGCCCTT AGGCCCCAGG GACTGGCTAA GTCGCCGTCA CTTAGACCTT

+3 T N Y T L T I S S L Q P E D F A T Y F C
      PstI
301 CAAATTACAC TCTCACCATC AGCAGCCTGC AGCCTGAAGA TTTTGCTACT TACTTTTGTG
   GTTTAATGTG AGAGTGGTAG TCGTCGGACG TCGGACTTCT AAAACGATGA ATGAAAACAG

+3 Q Q S D S L P I T F G Q G T R L D I Q G
361 AACAGTCTGA CAGTTTGCCG ATCACCTTCG GCCAAGGGAC ACGACTGGAC ATTCAAGGAG
   TTGTCAGACT GTCAAACGGC TAGTGGAAGC CGGTTCCCTG TGCTGACCTG TAAGTTCCCT

+3 G G G S G G G G S G G G G S E V Q L L E
      PvuII
421 GAGGAGGATC AGGTGGTGGT GGTAGCGGCG GCGGCGGCTC AGAGGTGCAG CTGCTCGAGT
   CTCCTCCTAG TCCACCACCA CCATCGCCGC CGCCGCCGAG TCTCCACGTC GACGAGCTCA

+3 S G G G V V Q P G R S L R L S C A A S G
481 CTGGGGGAGG CGTGGTCCAG CCTGGGAGGT CCCTGAGACT CTCCTGTGCA GCCTCTGGAT
   GACCCCTCC GCACCAGGTC GGACCCTCCA GGGACTCTGA GAGGACACGT CGGAGACCTA

+3 F T F S S Y G M H W V R Q A P G K G L E
541 TCACCTTCAG TAGCTATGGC ATGCACTGGG TCCGCCAGGC TCCAGGCAAG GGGCTGGAGT
   AGTGGAAGTC ATCGATACCG TACGTGACCC AGGCGGTCCG AGGTCCGTTC CCCGACCTCA

+3 W V A V I S Y D G S N K Y Y A D S V K G
      NdeI
601 GGGTGGCAGT TATATCATAT GATGGAAGTA ATAAATACTA TGCAGACTCC GTGAAGGGCC
   CCCACCGTCA ATATAGTATA CTACCTTCAT TATTTATGAT ACGTCTGAGG CACTTCCCGG

+3 R F T I S R D N S K N T L Y L Q M N S L
661 GATTACCAT CTCCAGAGAC AATTCCAAGA ACACGCTGTA TCTGCAAATG AACAGCCTGA
   CTAAGTGGTA GAGGTCTCTG TTAAGGTTCT TGTGCGACAT AGACGTTTAC TTGTCGGACT

+3 R A E D T A V Y Y C A K D M G W G S G W
721 GAGCTGAGGA CACGGCTGTG TATTACTGTG CGAAAGATAT GGGGTGGGGC AGTGGCTGGA
   CTCGACTCCT GTGCCGACAC ATAATGACAC GCTTTCTATA CCCCACCCCG TCACCGACCT

```


Figure 55a cont.

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+3 R P Y Y Y Y G M D V W G Q G T T V T V S
BspEI

781 GACCCTACTA CTACTACGGT ATGGACGTCT GGGGCCAAGG GACCACGGTC ACCGTCTCCT
CTGGGATGAT GATGATGCCA TACCTGCAGA CCCCGGTTCC CTGGTGCCAG TGGCAGAGGA

+3 S G T P L G D T T H T A S T K G P S V F
BspEI NheI

841 CCGGAACCCC GCTGGGTGAC ACCACCCACA CCGCTAGCAC CAAGGGCCCA TCGGTCTTCC
GGCCTTGGGG CGACCCACTG TGGTGGGTGT GGCATCGTG GTTCCCGGT AGCCAGAAGG

+3 P L A P S S K S T S G G T A A L G C L V
901 CCCTGGCACC CTCCTCCAAG AGCACCTCTG GGGGCACAGC GGCCCTGGGC TGCCTGGTCA
GGGACCGTGG GAGGAGGTTT TCGTGGAGAC CCCCGTGTCT CCGGGACCCG ACGGACCACT

+3 K D Y F P E P V T V S W N S G A L T S G
AgeI

961 AGGACTACTT CCCGAACCG GTGACGGTGT CGTGGAATC AGGCGCCCTG ACCAGCGGCG
TCCTGATGAA GGGGCTTGGC CACTGCCACA GCACCTTGA TCCGCGGGAC TGGTCGCCCG

+3 V H T F P A V L Q S S G L Y S L S S V V
1021 TGCACACCTT CCCGGCTGTC CTACAGTCTT CAGGACTCTA CTCCCTCAGC AGCGTGGTGA
ACGTGTGGAA GGGCCGACAG GATGTCAGGA GTCCTGAGAT GAGGGAGTCG TCGCACCACT

+3 T V P S S S L G T Q T Y I C N V N H K P
1081 CCGTGCCCTC CAGCAGCTTG GGCACCCAGA CCTACATCTG CAACGTGAAT CACAAGCCCA
GGCACGGGAG GTCGTGAAC CCGTGGGTCT GGATGTAGAC GTTGCACTTA GTGTTCTGGT

+3 S N T K V D K K V E P K S C D K T S G G
SpeI

1141 GCAACACCAA GGTGGACAAG AAAGTTGAGC CCAAATCTTG TGACAAAAC AGTGGAGGCG
CGTTGTGGTT CCACCTGTTC TTTCAACTCG GGTTTAGAAC ACTGTTTTGA TCACCTCCCG

+3 G G S A P A R S P S P S T Q P W E H V N
1201 GTGGGTCCGC ACCCGCCCGC TCGCCAGCC CCAGCAGCA GCCCTGGGAG CATGTGAATG
CACCCAGGCG TGGGCGGGCG AGCGGGTCGG GGTGTCGCT CCGGACCCCT GTACACTTAC

+3 A I Q E A R R L L N L S R D T A A E M N
1261 CCATCCAGGA GGCCCGGCGT CTCCTGAACC TGAGTAGAGA CACTGCTGCT GAGATGAATG
GGTAGTCTT CCGGGCCGCA GAGGACTTGG ACTCATCTCT GTGACGACGA CTCTACTTAC

+3 E T V E V I S E M F D L Q E P T C L Q T
1321 AAACAGTAGA AGTCATCTCA GAAATGTTT ACCTCCAGGA GCCGACCTGC CTACAGACCC
TTTGTCTCT TCAGTAGAGT CTTTACAAAC TGGAGTCTT CCGCTGGACG GATGTCTGGG

+3 R L E L Y K Q G L R G S L T K L K G P L
BsrGI

1381 GCCTGGAGCT GTACAAGCAG GGCCTGCGGG GCAGCCTCAC CAAGCTCAAG GGCCCTTGA
CGGACCTCGA CATGTTCTG CCGGACGCCC CGTCGGAGTG GTTCGAGTTC CCGGGGAAC

+3 T M M A S H Y K Q H C P P T P E T S C A
1441 CCATGATGGC CAGCCACTAC AAGCAGCACT GCCCTCCAAC CCCGAAACT TCCTGTGCAA
GGTACTACCG GTCGGTGATG TTCGTCTGTA CCGGAGGTTG GGGCCTTGA AGGACACGTT

+3 T Q I I T F E S F K E N L K D F L L V I
1501 CCCAGATTAT CACCTTTGAA AGTTTCAAAG AGAACCTGAA GGACTTTCTG CTTGTCTATC
GGGTCTAATA GTGGAACTT TCAAAGTTT TCTTGACTT CCGAAAGAC GAACAGTAGG

Figure 55a cont.

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+3 P F D C W E P V Q E H H H H H *

Sali

1561 CCTTTGACTG CTGGGAGCCA GTCCAGGAGC ATCATCACCA TCATCATTGA ~~~~~
GGAAACTGAC GACCCTCGGT CAGGTCCTCG TAGTAGTGGT AGTAGTAACT CAGCTGAATT

1621 AACAGCTCTG
TTGTCGAGAC

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+3 Figure 55b

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M' G W S C I I
EcoRI NcoI
~~~~~

1 TTTTCTTCTT CCATTTCAGG TGTCGTGAGG AATTCACCAT GGGATGGAGC TGTATCATCC  
AAAAAAAGAA GGTAAGTCC ACAGCACTCC TTAAGTGGTA CCCTACCTCG ACATAGTAGG

---

+3 L F L V A T A T G V H S E L Q M T Q S P  
~~~~~  
BsrGI SacI

61 TCTTCTTGGT AGCAACAGCT ACAGGTGTAC ACTCCGAGCT CCAGATGACC CAGTCTCCAT
AGAAGAACCA TCGTTGTGCA TGCCACATG TGAGGCTCGA GGTCTACTGG GTCAGAGGTA

+3 S S L S A S V G D R V T I T C R A S Q S
121 CCTCCCTGTC TGCATCTGTA GGAGACAGAG TCACCATCAC TTGCCGGGCA AGTCAGAGCA
GGAGGGACAG ACGTAGACAT CCTCTGTCTC AGTGGTAGTG AACGGCCCGT TCAGTCTCGT

+3 I S S Y L N W Y Q Q K P G Q P P K L L I
~~~~~  
SwaI

181 TTAGCAGCTA TTAAATTGG TATCAGCAGA AACCAGGACA GCCTCCTAAG CTGCTCATTT  
AATCGTCGAT AAATTTAACC ATAGTCGTCT TTGGTCCTGT CGGAGGATTG GACGAGTAA

---

+3 Y W A S T R E S G V P D R F S G S E S G  
~~~~~  
SmaI

241 ACTGGGCATC TACCCGGGAA TCCGGGGTCC CTGACCGATT CAGCGGCAGT GAATCTGGGA
TGACCCGTAG ATGGGCCCTT AGGCCCCAGG GACTGGCTAA GTCGCCGTCA CTTAGACCCT

+3 T N Y T L T I S S L Q P E D F A T Y F C
~~~~~  
PstI

301 CAAATTACAC TCTCACCATC AGCAGCCTGC AGCCTGAAGA TTTTGCTACT TACTTTTGTC  
GTTTAATGTG AGAGTGGTAG TCGTCGGACG TCGGACTTCT AAAACGATGA ATGAAAACAG

---

+3 Q Q S D S L P I T F G Q G T R L D I Q G  
361 AACAGTCTGA CAGTTTGCCG ATCACCTTCG GCCAAGGGAC ACGACTGGAC ATTCAAGGAG  
TTGTCAGACT GTCAAACGGC TAGTGGAAGC CGGTTCCCTG TGCTGACCTG TAAGTTCTCT

---

+3 G G G S G G G G S G G S E V Q L L E  
~~~~~  
PvuII

421 GAGGAGGATC AGGTGGTGGT GGTAGCGGCG GCGGCGGCTC AGAGGTGCAG CTGCTCGAGT
CTCCTCCTAG TCCACCACCA CCATCGCCGC CGCCGCCGAG TCTCCACGTC GACGAGCTCA

+3 S G G G V V Q P G R S L R L S C A A S G
481 CTGGGGGAGG CGTGGTCCAG CCTGGGAGGT CCCTGAGACT CTCCTGTGCA GCCTCTGGAT
GACCCCTCC GCACCAGGTC GGACCTCCA GGGACTCTGA GAGGACACGT CGGAGACCTA

+3 F T F S S Y G M H W V R Q A P G K G L E
541 TCACCTCAG TAGCTATGGC ATGCACTGGG TCCGCCAGGC TCCAGGCAAG GGGCTGGAGT
AGTGGAAGTC ATCGATACCG TACGTGACCC AGGCGGTCCG AGGTCCGTTC CCCGACCTCA

+3 W V A V I S Y D G S N K Y Y A D S V K G
~~~~~  
NdeI

601 GGGTGGCAGT TATATCATAT GATGGAAGTA ATAAATACTA TGCAGACTCC GTGAAGGGCC  
CCCACCGTCA ATATAGTATA CTACCTTCAT TATTTATGAT ACGTCTGAGG CACTTCCCCG

---

+3 R F T I S R D N S K N T L Y L Q M N S L  
661 GATTCACCAT CTCCAGAGAC AATTCCAAGA ACACGCTGTA TCTGCAAATG AACAGCCTGA  
CTAAGTGGTA GAGGTCTCTG TTAAGGTTCT TGTGCGACAT AGACGTTTAC TTGTCGGACT

---

+3 R A E D T A V Y Y C A K D M G W G S G W  
721 GAGCTGAGGA CACGGCTGTG TATTACTGTG CGAAAGATAT GGGGTGGGGC AGTGGCTGGA  
CTCGACTCCT GTGCCGACAC ATAATGACAC GCTTTCTATA CCCACCCCG TCACCGACCT

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Figure 55b cont.

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+3 R P Y Y Y Y G M D V W G Q G T T V T V S  
BspEI

781 GACCCTACTA CTACTACGGT ATGGACGTCT GGGGCCAAGG GACCACGGTC ACCGTCTCCT  
CTGGGATGAT GATGATGCCA TACCTGCAGA CCCCGGTTCC CTGGTGCCAG TGGCAGAGGA

+3 S G T P L G D T T H T R T V A A P S V F  
BspEI BsiWI

841 CCGGAACCCC GCTGGGTGAC ACCACCCACA CCCGTACGGT GGCTGCACCA TCTGTCTTCA  
GGCCTTGGGG CGACCCACTG TGGTGGGTGT GGGCATGCCA CCGACGTGGT AGACAGAAGT

+3 I F P P S D E Q L K S G T A S V V C L L  
901 TCTTCCC GCC ATCTGATGAG CAGTTGAAAT CTGGAAGTGC CTCTGTTGTG TGCCTGCTGA  
AGAAGGGCGG TAGACTACTC GTCAACTTTA GACCTTGACG GAGACAACAC ACGGACGACT

+3 N N F Y P R E A K V Q W K V D N A L Q S  
961 ATAATTCTA TCCCAGAGAG GCCAAAGTAC AGTGGAAGGT GGATAACGCC CTCCAATCGG  
TATTGAAGAT AGGGTCTCTC CGGTTTCATG TCACCTTCCA CCTATTGCGG GAGGTTAGCC

+3 G N S Q E S V T E Q D S K D S T Y S L S  
1021 GTAATTCCCA GGAGAGTGTC ACAGAGCAGG ACAGCAAGGA CAGCACCTAC AGCCTCAGCA  
CATTGAGGGT CCTCTCACAG TGTCTCGTCC TGTCGTTTCTT GTCGTGGATG TCGGAGTCGT

+3 S T L T L S K A D Y E K H K V Y A C E V  
1081 GCACCCTGAC GCTGAGCAAA GCAGACTACG AGAAACACAA AGTCTACGCC TGCGAAGTCA  
CGTGGGACTG CGACTCGTTT CGTCTGATGC TCTTTGTGTT TCAGATGCGG ACGCTTCAGT

+3 T H Q G L S S P V T K S F N R G E C S G  
SacI

1141 CCCATCAGGG CCTGAGCTCG CCCGTCACAA AGAGCTTCAA CAGGGGAGAG TGTTCAAGGAG  
GGGTAGTCCC GGACTCGAGC GGGCAGTGTT TCTCGAAGTT GTCCCCTCTC ACAAGTCCTC

+3 G G G S A P T S S S T K K T Q L Q L E H  
1201 GCGGTGGGTC TGCACCTACT TCAAGTTCTA CAAAGAAAAC ACAGCTACAA CTGGAGCATT  
CGCCACCCAG ACGTGGATGA AGTTCAAGAT GTTCTTTTGT TGTCGATGTT GACCTCGTAA

+3 L L L D L Q M I L N G I N N Y K N P K L  
1261 TACTGCTGGA TTTACAGATG ATTTTGAATG GAATTAATAA TTACAAGAAT CCCAAACTCA  
ATGACGACCT AAATGTCTAC TAAACTTAC CTTAATTATT AATGTTCTTA GGGTTTGAGT

+3 T R M L T F K F Y M P K K A T E L K H L  
1321 CCAGGATGCT CACATTTAAG TTTTACATGC CCAAGAAGGC CACAGAAGTGC AAACATCTTC  
GGTCCTACGA GTGTAAATTC AAAATGTACG GGTCTTCCG GTGTCTTGAC TTTGTAGAAG

+3 Q C L E E E L K P L E E V L N L A Q S K  
XbaI

1381 AGTGTCTAGA AGAAGAACTC AAACCTCTGG AGGAAGTGCT AAATTTAGCT CAAAGCAAAA  
TCACAGATCT TCTTCTTGAG TTTGGAGACC TCCTTCACGA TTAAATCGA GTTTCGTTTT

+3 N F H L R P R D L I S N I N V I V L E L  
1441 ACTTTCATT AAGACCCAGG GACTTAATCA GCAATATCAA CGTAATAGTT CTGGAAGTAA  
TGAAAGTGAA TTCTGGGTCC CTGAATTAGT CGTTATAGTT GCATTATCAA GACCTTGATT

+3 K G S E T T F M C E Y A D E T A T I V E  
1501 AGGGATCTGA AACAACATTC ATGTGTGAAT ATGCTGATGA GACAGCAACC ATTGTAGAAT  
TCCCTAGACT TTGTTGTAAG TACACACTTA TACGACTACT CTGTCGTTGG TAACATCTTA

+3 F L N R W I T F C Q S I I S T L T \* \*  
SalI

1561 TTCTGAACAG ATGGATTACC TTTTGTCAAA GCATCATCTC AACACTAACT TGATAAGTCG  
AAGACTTGTC TACCTAATGG AAAACAGTTT CGTAGTAGAG TTGTGATTGA ACTATTACAG

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Figure 55b cont.

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SalI

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1621 ACTTAAAACA  
TGAATTTTGT

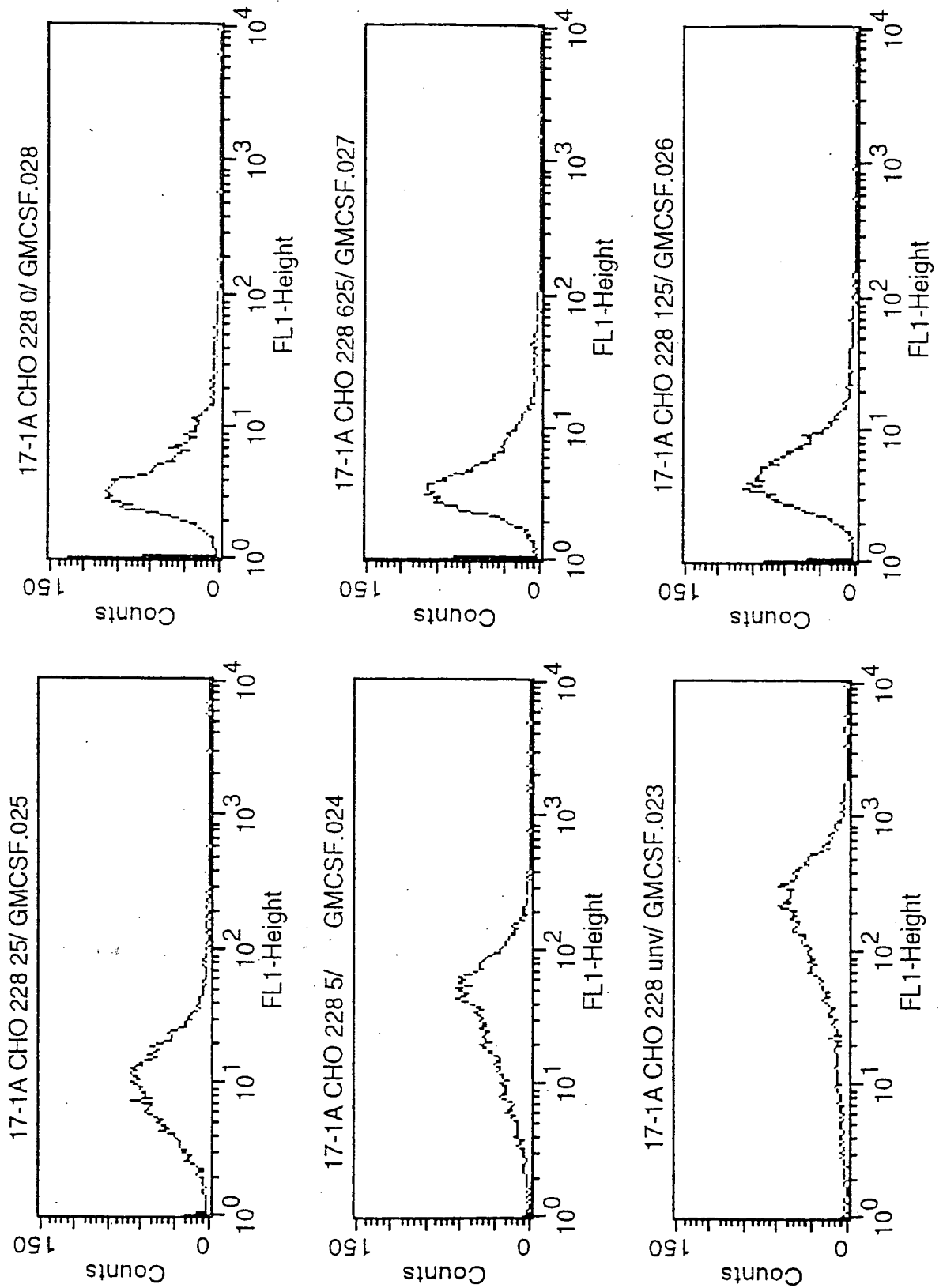
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# Association of EpCAM Binding and GM-CSF in Heterominibody

FIGURE 56

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Figure 57

### Physical Linkage of Anti-EpCAM Activity with IL-2 and GM-CSF

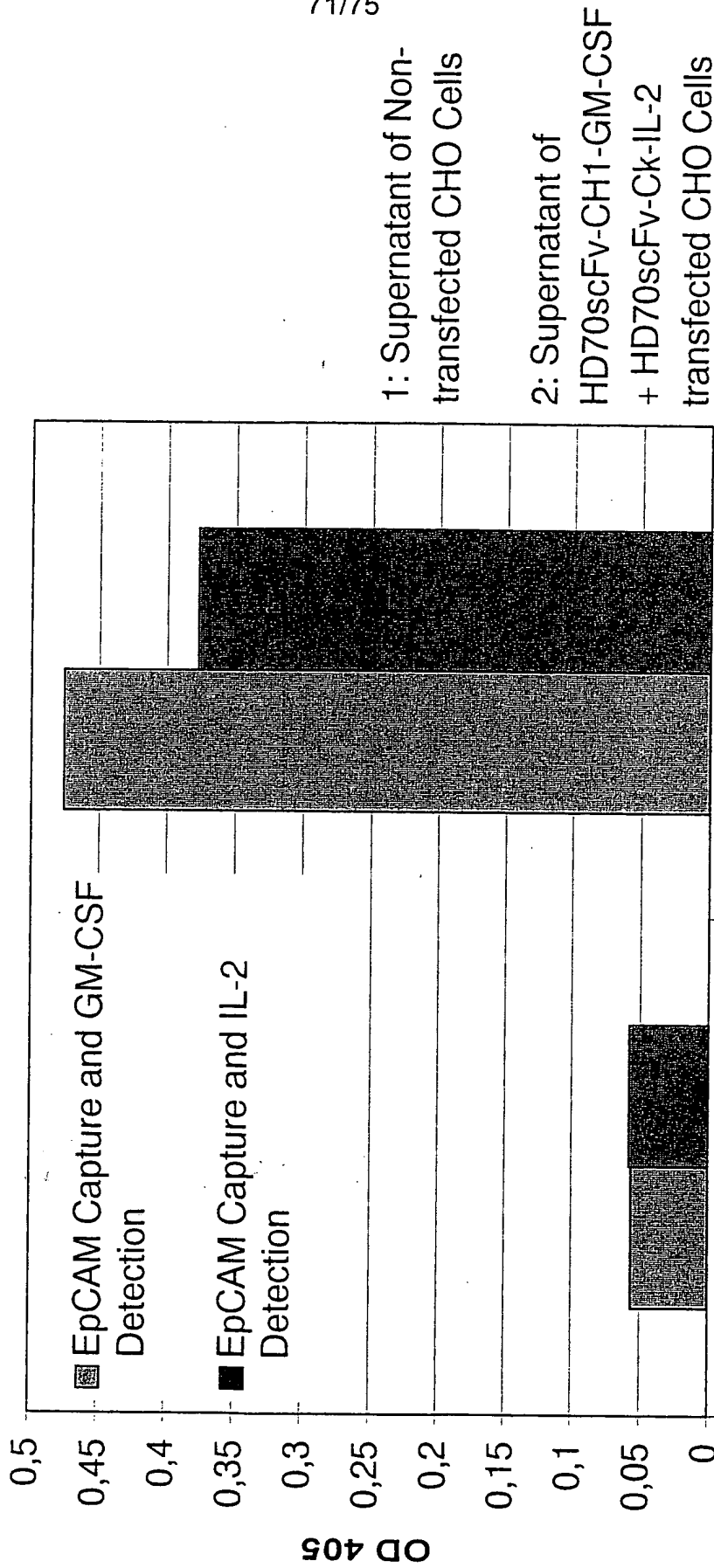
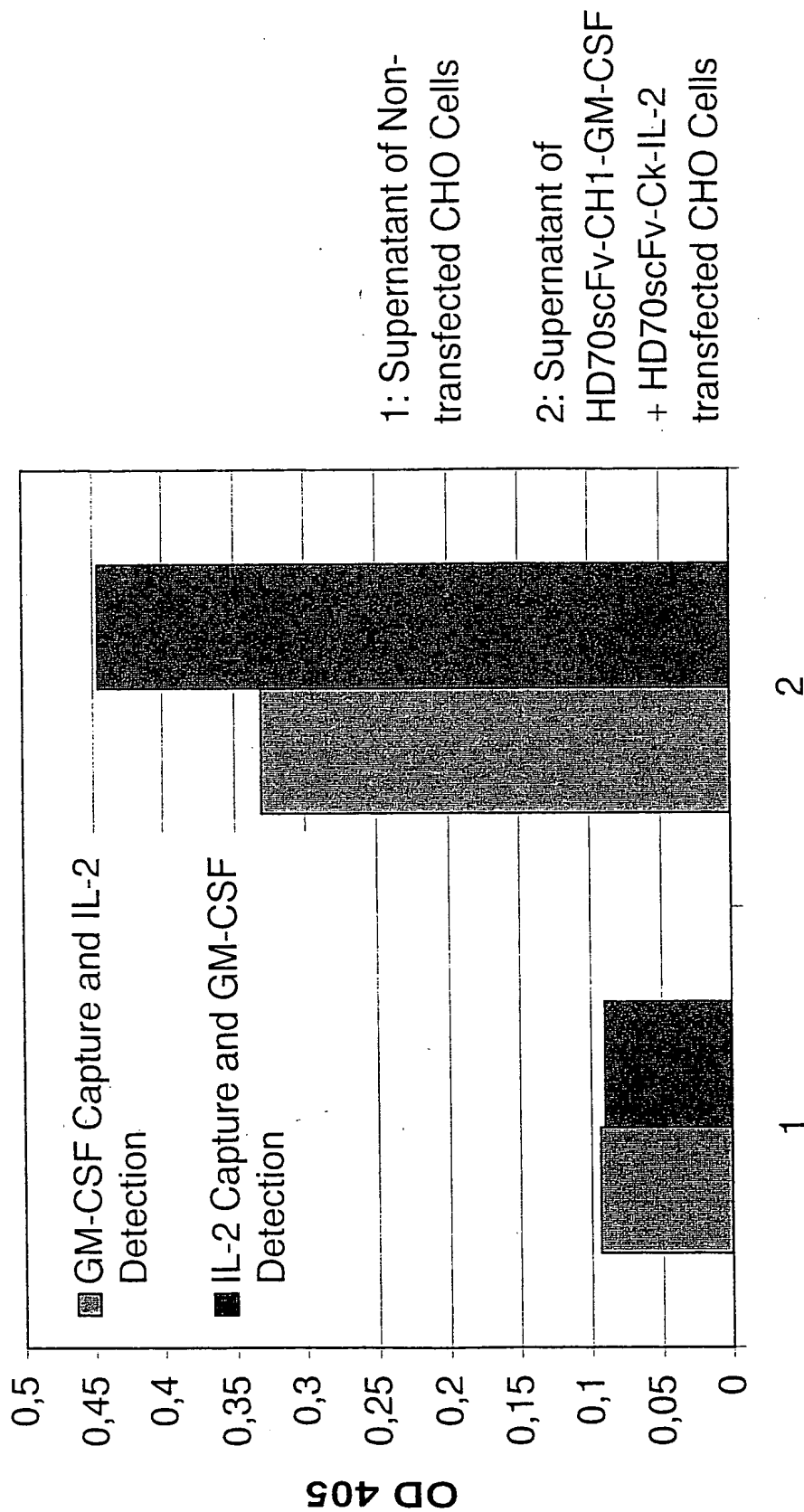


Figure 58

# Physical Linkage of IL-2 with GM-CSF in Heterominibody





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Figure 59

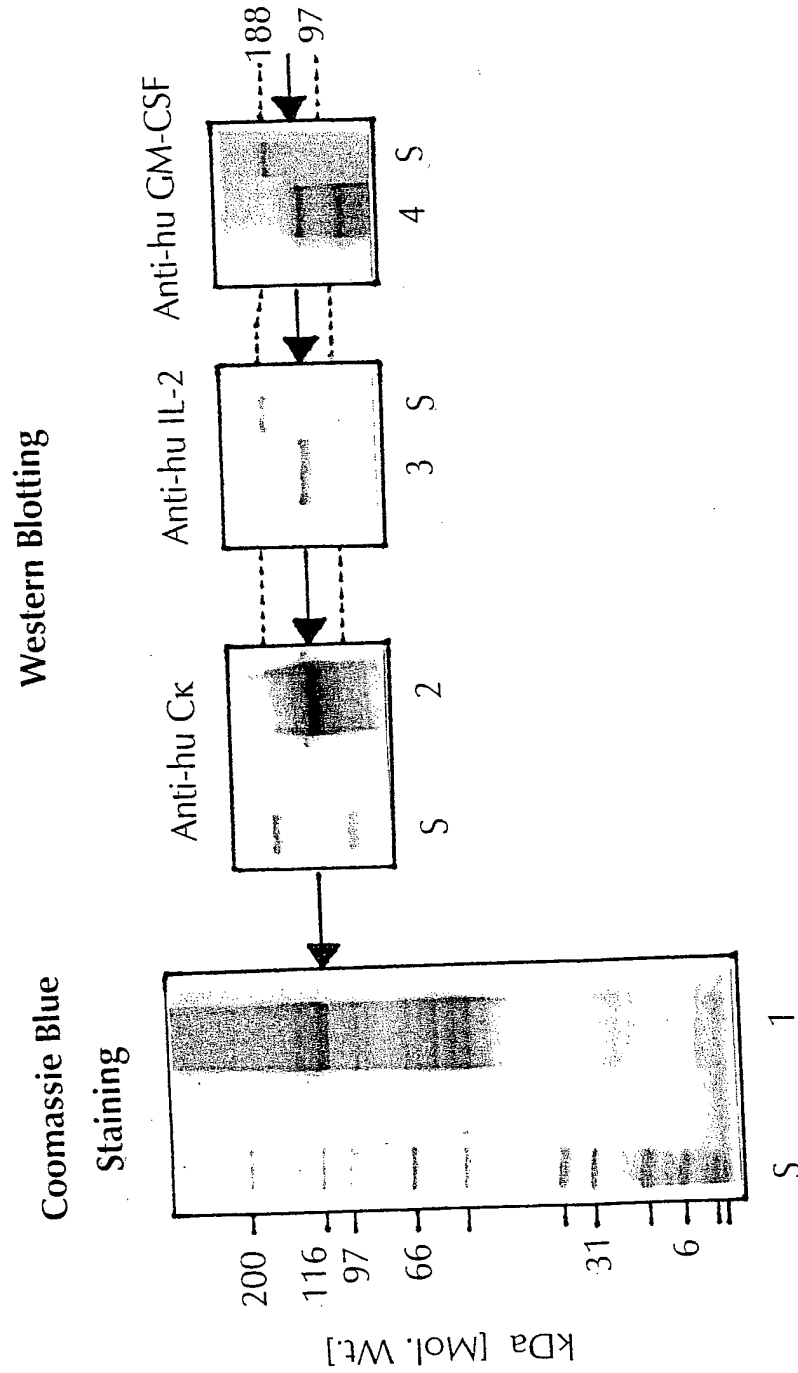
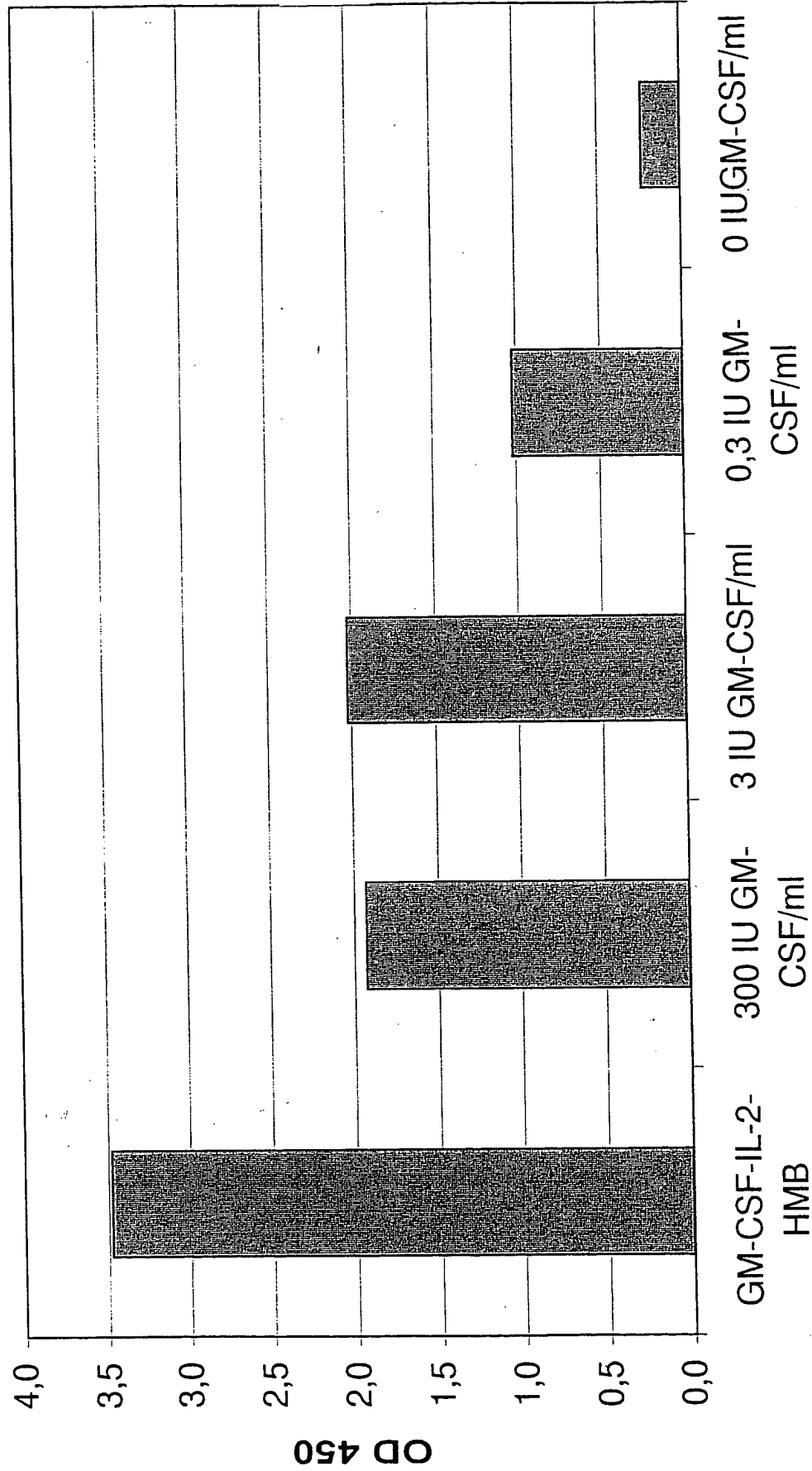


Figure 60

# Bioactivity of GM-CSF in Heterominibody Format



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# Bioactivity of IL-2 in Heteroninibody Format

Figure 61

